STIC-Biotech/ChemLib

58015

MSJ

From: Huff, Sheela
Sent: Thursday, January 10, 2002 12:34 PM
To: STIC-Biotech/ChemLib
Subject: search request for 09/767424

THIS IS NOT A SEQEUNCE SEARCH.

Please search the use of temozolomide (which is 3,4-dihydro-3-methyl-4-oxoimidazo-[5,1-d]1,2,3,4-tetrazin-8-carboximide) and pegylated interferon alpha to treat cancers.
Please note that the claim requires both compounds to treat cancers.

inventor: Sara L. Zaknoen
Title: Combination therapy for cancer

Thanks--

Sheela Huff
Art Unit 1642
CM1-8B07
mailbox 8E12
305-7866

d cn rn

Searcher: Thom Larson
Phone: 308-7309
Location: 12 C 14
Date Picked Up: 1/18/02
Date Completed: 1/23/02
Searcher Prep/Review: 150
Clerical: _____
Online time: 322

TYPE OF SEARCH:
NA Sequences: _____
AA Sequences: _____
Structures: _____
Bibliographic: ✓
Litigation: _____
Full text: _____
Patent Family: _____
Other: _____

VENDOR/COST(where applic.)
STN: #716
DIALOG: _____
Questel/Orbit: _____
DRLink: _____
Lexis/Nexis: _____
Sequence Sys.: _____
WWW/Internet: N E M PDP
Other (specify): WEST-NC

=> file reg; d que l1; d l1 2; d que l4; d l4

FILE 'REGISTRY' ENTERED AT 18:10:13 ON 22 JAN 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 20 JAN 2002 HIGHEST RN 385365-97-9
DICTIONARY FILE UPDATES: 20 JAN 2002 HIGHEST RN 385365-97-9

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

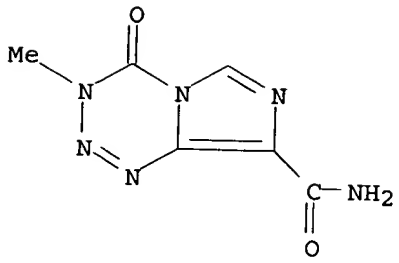
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

L1 2 SEA FILE=REGISTRY ABB=ON TEMOZOLOMIDE

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN 85622-93-1 REGISTRY
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN CCRG 81045
CN M and B 39831
CN MB 39831
CN Methazolastone
CN NSC 362856
CN Sch 52365
CN Temodal
CN **Temozolomide**
FS 3D CONCORD
DR 97716-75-1
MF C6 H6 N6 O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CIN, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PHARMASEARCH, PROMT, RTECS*, SYNTHLINE, TOXCENTER, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

212 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
214 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 (735) SEA FILE=REGISTRY ABB=ON INTERFERON ALPHA
L3 (5699) SEA FILE=REGISTRY ABB=ON PEG OR POLYETHYLENE GLYCOL OR PEGYLATED
L4 1 SEA FILE=REGISTRY ABB=ON L2 AND L3

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 215647-85-1 REGISTRY
CN **Interferon .alpha.-2b (human), pegylated (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN Peginterferon alfa-2b
CN PegIntron
CN Sch 54031
MF Unspecified
CI MAN
SR US Adopted Names Council
LC STN Files: ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CAPLUS, EMBASE, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TQ DATE)

```
=> file medline; d que l14; d que l25; s l14 or l25

FILE 'MEDLINE' ENTERED AT 18:10:31 ON 22 JAN 2002

 FILE LAST UPDATED: 21 JAN 2002 (20020121/UP). FILE COVERS 1958 TO DATE.

 On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE now contains IN-PROCESS records. See HELP CONTENT for details.

 MEDLINE is now updated 4 times per week. A new current-awareness alert
 frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

 The OLDMEDLINE file segment now contains data from 1958 through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in the
 Basic Index. See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.


L5   (         7)SEA FILE=MEDLINE ABB=ON  TEMOLOZOMID## OR TEMOLDAL# OR TEMODAR
                  OR METHAZOLASTON##
L6   (        11)SEA FILE=MEDLINE ABB=ON  CCRG 81045 OR ("M AND B" OR MB) (W)
                  39831 OR NSC 362856 OR SCH 52365
L7   (       190)SEA FILE=MEDLINE ABB=ON  85622-93-1
L8   (       190)SEA FILE=MEDLINE ABB=ON  L5 OR L6 OR L7
L9   (        19)SEA FILE=MEDLINE ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
                  PEGINTRON OR PEG-INTRON OR SCH 54031
L10  (     70592)SEA FILE=MEDLINE ABB=ON  INTERFERON#
L11  (      9481)SEA FILE=MEDLINE ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
                  POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L12  (      6807)SEA FILE=MEDLINE ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L13  (        74)SEA FILE=MEDLINE ABB=ON  L9 OR (L10 (3A) (L11 OR L12))
L14           0 SEA FILE=MEDLINE ABB=ON  L8 AND L13



L15  (        19)SEA FILE=MEDLINE ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
                  PEGINTRON OR PEG-INTRON OR SCH 54031
L16  (     70592)SEA FILE=MEDLINE ABB=ON  INTERFERON#
L17  (      9481)SEA FILE=MEDLINE ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
                  POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L18  (      6807)SEA FILE=MEDLINE ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L19  (        74)SEA FILE=MEDLINE ABB=ON  L15 OR (L16 (3A) (L17 OR L18))
L20  (    236549)SEA FILE=MEDLINE ABB=ON  CHEMOTHERAP? OR ANTITUMOR OR ANTINEOPL
                  ASTIC OR ANAPLASTIC OR ONCOLOGY
L21  (    954862)SEA FILE=MEDLINE ABB=ON  CANCER# OR TUMOR# OR MEOPLASM# OR
                  CARCINOMA# OR ASTROCYTOMA#
L22  (   1053579)SEA FILE=MEDLINE ABB=ON  L20 OR L21
L23  (        13)SEA FILE=MEDLINE ABB=ON  L19 AND L22
L24  (     19568)SEA FILE=MEDLINE ABB=ON  ANTIVIRAL AGENTS/CT
L25           8 SEA FILE=MEDLINE ABB=ON  L23 NOT L24

L241          8 L14 OR L25
```

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TL

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=> file cancerlit; d que l37; d que l49; s l37 or l49

FILE 'CANCERLIT' ENTERED AT 18:10:39 ON 22 JAN 2002

 FILE COVERS 1963 TO 14 Jun 2001 (20010614/ED)

 CANCERLIT thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2000 vocabulary.  Enter HELP THESAURUS for details.

 This file contains CAS Registry Numbers for easy and accurate substance
 identification.


L26 (         1)SEA FILE=CANCERLIT ABB=ON  TEMOLOZOMID## OR TEMOLDAL# OR
                TEMODAR OR METHAZOLASTON##
L27 (        16)SEA FILE=CANCERLIT ABB=ON  CCRG 81045 OR ("M AND B" OR MB) (W)
                39831 OR NSC 362856 OR SCH 52365
L28 (       197)SEA FILE=CANCERLIT ABB=ON  85622-93-1
L29 (       198)SEA FILE=CANCERLIT ABB=ON  L26 OR L27 OR L28
L30 (         7)SEA FILE=CANCERLIT ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
                PEGINTRON OR PEG-INTRON OR SCH 54031
L31 (     62162)SEA FILE=CANCERLIT ABB=ON  INTERFERON#
L32 (      1671)SEA FILE=CANCERLIT ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
                POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L33 (      1184)SEA FILE=CANCERLIT ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L34 (        29)SEA FILE=CANCERLIT ABB=ON  L31. (3A) (L32 OR L33)
L35 (         0)SEA FILE=CANCERLIT ABB=ON  215647-85-1
L36 (        29)SEA FILE=CANCERLIT ABB=ON  L30 OR L34 OR L35
L37           0 SEA FILE=CANCERLIT ABB=ON  L29 AND L36


L38 (         7)SEA FILE=CANCERLIT ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
                PEGINTRON OR PEG-INTRON OR SCH 54031
L39 (     62162)SEA FILE=CANCERLIT ABB=ON  INTERFERON#
L40 (      1671)SEA FILE=CANCERLIT ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
                POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L41 (      1184)SEA FILE=CANCERLIT ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L42 (        29)SEA FILE=CANCERLIT ABB=ON  L39 (3A) (L40 OR L41)
L43 (         0)SEA FILE=CANCERLIT ABB=ON  215647-85-1
L44 (        29)SEA FILE=CANCERLIT ABB=ON  L38 OR L42 OR L43
L45 (    240533)SEA FILE=CANCERLIT ABB=ON  CHEMOTHERAP? OR ANTITUMOR OR
               ANTINEOPLASTIC OR ANAPLASTIC OR ONCOLOGY
L46 (    890552)SEA FILE=CANCERLIT ABB=ON  CANCER# OR TUMOR# OR MEOPLASM# OR
               CARCINOMA# OR ASTROCYTOMA#
L47 (         5)SEA FILE=CANCERLIT ABB=ON  L44 AND (L45 OR L46)
L48 (      5748)SEA FILE=CANCERLIT ABB=ON  ANTIVIRAL AGENTS/CT
L49           2 SEA FILE=CANCERLIT ABB=ON  L47 NOT L48


L242          2 L37 OR L49
```

```
=> file caplus; d que 162; d que 176; d que 190; s 162 or 176 or 190

FILE 'CAPLUS' ENTERED AT 18:10:45 ON 22 JAN 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 22 Jan 2002  VOL 136 ISS 4
FILE LAST UPDATED: 20 Jan 2002  (20020120/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

  This file supports REG1stRY for direct browsing and searching of
  all substance data from the REGISTRY file.  Enter HELP FIRST for
  more information.

CAplus now provides online access to patents and literature
covered in CA from 1907 to the present.  Bibliographic
information and abstracts were added in 2001 for over 3.8
million records from 1907-1966.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

The CA Lexicon is now available in the Controlled Term (/CT) field.
Enter HELP LEXICON for full details.

Attention, the CA Lexicon is the copyrighted intellectual property of
the American Chemical Society and is provided to assist you in
searching databases on STN.  Any dissemination, distribution, copying,
or storing of this information, without the prior written consent of
CAS, is strictly prohibited.

L50 (         5) SEA FILE=CAPLUS ABB=ON  TEMOLOZOMID## OR TEMOLDAL# OR TEMODAR
                 OR METHAZOLASTON##
L51 (       211) SEA FILE=CAPLUS ABB=ON  85622-93-1/RN
L52 (        10) SEA FILE=CAPLUS ABB=ON  CCRG 81045 OR ("M AND B" OR MB) (W)
                 39831 OR NSC 362856 OR SCH 52365
L53 (       211) SEA FILE=CAPLUS ABB=ON  L50 OR L51 OR L52
L54 (        26) SEA FILE=CAPLUS ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
                 PEGINTRON OR PEG-INTRON OR SCH 54031
L55 (     59321) SEA FILE=CAPLUS ABB=ON  INTERFERON#
L56 (     78559) SEA FILE=CAPLUS ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
                 POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L57 (     27348) SEA FILE=CAPLUS ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L58 (     93749) SEA FILE=CAPLUS ABB=ON  L56 OR L57
L59 (       110) SEA FILE=CAPLUS ABB=ON  L55 (3A) L58
L60 (         3) SEA FILE=CAPLUS ABB=ON  215647-85-1/RN
L61 (       114) SEA FILE=CAPLUS ABB=ON  L54 OR L59 OR L60
L62           (1) SEA FILE=CAPLUS ABB=ON  L53 AND L61
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See pp. 20-21

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L63 (        26)SEA FILE=CAPLUS ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
               PEGINTRON OR PEG-INTRON OR SCH 54031
L64 (     59321)SEA FILE=CAPLUS ABB=ON  INTERFERON#
L65 (     78559)SEA FILE=CAPLUS ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
               POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L66 (     27348)SEA FILE=CAPLUS ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L67 (     93749)SEA FILE=CAPLUS ABB=ON  L65 OR L66
L68 (       110)SEA FILE=CAPLUS ABB=ON  L64 (3A) L67
L69 (         3)SEA FILE=CAPLUS ABB=ON  215647-85-1/RN
L70 (       114)SEA FILE=CAPLUS ABB=ON  L63 OR L68 OR L69
L71 (    140399)SEA FILE=CAPLUS ABB=ON  CHEMOTHERAP? OR ANTITUMOR OR ANTINEOPLA
               STIC OR ANAPLASTIC OR ONCOLOGY
L72 (    403644)SEA FILE=CAPLUS ABB=ON  CANCER# OR TUMOR# OR MEOPLASM# OR
               CARCINOMA# OR ASTROCYTOMA#
L73 (    462898)SEA FILE=CAPLUS ABB=ON  L71 OR L72
L74 (        22)SEA FILE=CAPLUS ABB=ON  L70 AND L73
L75 (    127422)SEA FILE=CAPLUS ABB=ON  (VIRUS## OR ANTIVIRAL# OR HEPATITIS)/TI

L76          18 SEA FILE=CAPLUS ABB=ON  L74 NOT L75


L77 (         5)SEA FILE=CAPLUS ABB=ON  TEMOLOZOMID## OR TEMOLDAL# OR TEMODAR
               OR METHAZOLASTON##
L78 (       211)SEA FILE=CAPLUS ABB=ON  85622-93-1/RN
L79 (        10)SEA FILE=CAPLUS ABB=ON  CCRG 81045 OR ("M AND B" OR MB) (W)
               39831 OR NSC 362856 OR SCH 52365
L80 (       211)SEA FILE=CAPLUS ABB=ON  L77 OR L78 OR L79
L81 (        26)SEA FILE=CAPLUS ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
               PEGINTRON OR PEG-INTRON OR SCH 54031
L82 (     59321)SEA FILE=CAPLUS ABB=ON  INTERFERON#
L83 (     78559)SEA FILE=CAPLUS ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
               POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L84 (     27348)SEA FILE=CAPLUS ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L85 (     93749)SEA FILE=CAPLUS ABB=ON  L83 OR L84
L86 (       110)SEA FILE=CAPLUS ABB=ON  L82 (3A) L85
L87 (         3)SEA FILE=CAPLUS ABB=ON  215647-85-1/RN
L88 (       114)SEA FILE=CAPLUS ABB=ON  L81 OR L86 OR L87
L89 (         8)SEA FILE=CAPLUS ABB=ON  ("ZAKNOEN S"/AU OR "ZAKNOEN SARA"/AU
               OR "ZAKNOEN SARA L"/AU)
L90           4 SEA FILE=CAPLUS ABB=ON  (L80 OR L88) AND L89


L243         21 L62 OR L76 OR L90

=> file biosis; d que l103; d que l118; s l103 or l118

FILE 'BIOSIS' ENTERED AT 18:10:54 ON 22 JAN 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 16 January 2002 (20020116/ED)
```

The BIOSIS file has been reloaded. Enter HELP RLOAD and HELP REINDEXING for details.

```
L91 (         7)SEA FILE=BIOSIS ABB=ON  TEMOLOZOMID## OR TEMOLDAL# OR TEMODAR
              OR METHAZOLASTON##
L92 (        19)SEA FILE=BIOSIS ABB=ON  CCRG 81045 OR ("M AND B" OR MB) (W)
              39831 OR NSC 362856 OR SCH 52365
L93 (       276)SEA FILE=BIOSIS ABB=ON  85622-93-1
L94 (       280)SEA FILE=BIOSIS ABB=ON  L91 OR L92 OR L93
L95 (        53)SEA FILE=BIOSIS ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
              PEGINTRON OR PEG-INTRON OR SCH 54031
L96 (     90443)SEA FILE=BIOSIS ABB=ON  INTERFERON#
L97 (     15604)SEA FILE=BIOSIS ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
              POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L98 (     10059)SEA FILE=BIOSIS ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L99 (     20025)SEA FILE=BIOSIS ABB=ON  L97 OR L98
L100(       117)SEA FILE=BIOSIS ABB=ON  L96 (3A) L99
L101(         1)SEA FILE=BIOSIS ABB=ON  215647-85-1
L102(       140)SEA FILE=BIOSIS ABB=ON  L95 OR L100 OR L101
L103          0 SEA FILE=BIOSIS ABB=ON  L94 AND L102


L104(        53)SEA FILE=BIOSIS ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
              PEGINTRON OR PEG-INTRON OR SCH 54031
L105(     90443)SEA FILE=BIOSIS ABB=ON  INTERFERON#
L106(     15604)SEA FILE=BIOSIS ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
              POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L107(     10059)SEA FILE=BIOSIS ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L108(     20025)SEA FILE=BIOSIS ABB=ON  L106 OR L107
L109(       117)SEA FILE=BIOSIS ABB=ON  L105 (3A) L108
L110(         1)SEA FILE=BIOSIS ABB=ON  215647-85-1
L111(       140)SEA FILE=BIOSIS ABB=ON  L104 OR L109 OR L110
L112(    547761)SEA FILE=BIOSIS ABB=ON  CHEMOTHERAP? OR ANTITUMOR OR ANTINEOPLA
              STIC OR ANAPLASTIC OR ONCOLOGY
L113(    962815)SEA FILE=BIOSIS ABB=ON  CANCER# OR TUMOR# OR MEOPLASM# OR
              CARCINOMA# OR ASTROCYTOMA#
L114(        21)SEA FILE=BIOSIS ABB=ON  L111 AND (L112 OR L113)
L115(     89266)SEA FILE=BIOSIS ABB=ON  HEPATITIS
L116(        14)SEA FILE=BIOSIS ABB=ON  L114 NOT L115
L117(     29641)SEA FILE=BIOSIS ABB=ON  (ENCEPHALITIS OR PERMEABILITY)/TI
L118         12 SEA FILE=BIOSIS ABB=ON  L116 NOT L117


L244         12 L103 OR L118

=> file biotechno; d que l131; d que l144; s l131 or l144

FILE 'BIOTECHNO' ENTERED AT 18:10:58 ON 22 JAN 2002
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FILE LAST UPDATED: 15 JAN 2002      <20020115/UP>
FILE COVERS 1980 TO DATE.

>>>  SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
     /CT AND BASIC INDEX  <<<
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L119(         9)SEA FILE=BIOTECHNO ABB=ON  TEMOLOZOMID## OR TEMOLDAL# OR
                TEMODAR OR METHAZOLASTON##
L120(         2)SEA FILE=BIOTECHNO ABB=ON  CCRG 81045 OR ("M AND B" OR MB) (W)
                39831 OR NSC 362856 OR SCH 52365
L121(       134)SEA FILE=BIOTECHNO ABB=ON  85622-93-1
L122(       135)SEA FILE=BIOTECHNO ABB=ON  L119 OR L120 OR L121
L123(        47)SEA FILE=BIOTECHNO ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
                PEGINTRON OR PEG-INTRON OR SCH 54031
L124(     39162)SEA FILE=BIOTECHNO ABB=ON  INTERFERON#
L125(      3874)SEA FILE=BIOTECHNO ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
                POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L126(      3802)SEA FILE=BIOTECHNO ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L127(      2204)SEA FILE=BIOTECHNO ABB=ON  L125 AND L126
L128(        54)SEA FILE=BIOTECHNO ABB=ON  L124 (3A) L127
L129(         1)SEA FILE=BIOTECHNO ABB=ON  215647-85-1
L130(        87)SEA FILE=BIOTECHNO ABB=ON  L123 OR L128 OR L129
L131          0 SEA FILE=BIOTECHNO ABB=ON  L122 AND L130


L132(        47)SEA FILE=BIOTECHNO ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
                PEGINTRON OR PEG-INTRON OR SCH 54031
L133(     39162)SEA FILE=BIOTECHNO ABB=ON  INTERFERON#
L134(      3874)SEA FILE=BIOTECHNO ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
                POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L135(      3802)SEA FILE=BIOTECHNO ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L136(      2204)SEA FILE=BIOTECHNO ABB=ON  L134 AND L135
L137(        54)SEA FILE=BIOTECHNO ABB=ON  L133 (3A) L136
L138(         1)SEA FILE=BIOTECHNO ABB=ON  215647-85-1
L139(        87)SEA FILE=BIOTECHNO ABB=ON  L132 OR L137 OR L138
L140(     33605)SEA FILE=BIOTECHNO ABB=ON  CHEMOTHERAP? OR ANTITUMOR OR
                ANTINEOPLASTIC OR ANAPLASTIC OR ONCOLOGY
L141(    179406)SEA FILE=BIOTECHNO ABB=ON  CANCER# OR TUMOR# OR MEOPLASM# OR
                CARCINOMA# OR ASTROCYTOMA#
L142(        26)SEA FILE=BIOTECHNO ABB=ON  L139 AND (L140 OR L141)
L143(     24416)SEA FILE=BIOTECHNO ABB=ON  FOLATE OR HEPATITIS
L144         13 SEA FILE=BIOTECHNO ABB=ON  L142 NOT L143


L245         13 L131 OR L144

=> file embase; dque l157; dque l171; s l157 or l171

FILE 'EMBASE' ENTERED AT 18:11:03 ON 22 JAN 2002
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 FILE COVERS 1974 TO 17 Jan 2002 (20020117/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=>  d que l157; d que l171; s l157 or l171

L145(        22)SEA FILE=EMBASE ABB=ON  TEMOLOZOMID## OR TEMOLDAL# OR TEMODAR
              OR METHAZOLASTON##
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L146(       505)SEA FILE=EMBASE ABB=ON  85622-93-1
L147(        28)SEA FILE=EMBASE ABB=ON  CCRG 81045 OR ("M AND B" OR MB) (W)
               39831 OR NSC 362856 OR SCH 52365
L148(       509)SEA FILE=EMBASE ABB=ON  L145 OR L146 OR L147
L149(        57)SEA FILE=EMBASE ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
               PEGINTRON OR PEG-INTRON OR SCH 54031
L150(     81013)SEA FILE=EMBASE ABB=ON  INTERFERON#
L151(      9463)SEA FILE=EMBASE ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
               POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L152(     13489)SEA FILE=EMBASE ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L153(     17032)SEA FILE=EMBASE ABB=ON  L151 OR L152
L154(        82)SEA FILE=EMBASE ABB=ON  L150 (3A) L153
L155(         1)SEA FILE=EMBASE ABB=ON  215647-85-1
L156(       115)SEA FILE=EMBASE ABB=ON  L149 OR L154 OR L155
L157          0 SEA FILE=EMBASE ABB=ON  L148 AND L156


L158(        57)SEA FILE=EMBASE ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
               PEGINTRON OR PEG-INTRON OR SCH 54031
L159(     81013)SEA FILE=EMBASE ABB=ON  INTERFERON#
L160(      9463)SEA FILE=EMBASE ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
               POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L161(     13489)SEA FILE=EMBASE ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L162(     17032)SEA FILE=EMBASE ABB=ON  L160 OR L161
L163(        82)SEA FILE=EMBASE ABB=ON  L159 (3A) L162
L164(         1)SEA FILE=EMBASE ABB=ON  215647-85-1
L165(       115)SEA FILE=EMBASE ABB=ON  L158 OR L163 OR L164
L166(    229190)SEA FILE=EMBASE ABB=ON  CHEMOTHERAP? OR ANTITUMOR OR ANTINEOPLA
               STIC OR ANAPLASTIC OR ONCOLOGY
L167(    967248)SEA FILE=EMBASE ABB=ON  CANCER# OR TUMOR# OR MEOPLASM# OR
               CARCINOMA# OR ASTROCYTOMA#
L168(   1017850)SEA FILE=EMBASE ABB=ON  L166 OR L167
L169(        34)SEA FILE=EMBASE ABB=ON  L165 AND L168
L170(     78154)SEA FILE=EMBASE ABB=ON  HEPATITIS
L171          9 SEA FILE=EMBASE ABB=ON  L169 NOT L170


L246          9 L157 OR L171

=> file drugu; d que l183; d que l195; s l183 or l195

FILE 'DRUGU' ENTERED AT 18:11:48 ON 22 JAN 2002
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FILE LAST UPDATED: 18 JAN 2002      <20020118/UP>
>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<

>>>  SDI'S MAY BE RUN WEEKLY OR MONTHLY AS OF JUNE 2001.  <<<
>>>  (WEEKLY IS THE DEFAULT). FOR PRICING INFORMATION     <<<
>>>  SEE HELP COST                                        <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<


L172(         5)SEA FILE=DRUGU ABB=ON  TEMOLOZOMID## OR TEMOLDAL# OR TEMODAR
               OR METHAZOLASTON##
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L173(        26)SEA FILE=DRUGU ABB=ON  CCRG 81045 OR ("M AND B" OR MB) (W)
               39831 OR NSC 362856 OR SCH 52365
L174(       255)SEA FILE=DRUGU ABB=ON  85622-93-1
L175(       269)SEA FILE=DRUGU ABB=ON  L172 OR L173 OR L174
L176(        23)SEA FILE=DRUGU ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
               PEGINTRON OR PEG-INTRON OR SCH 54031
L177(     22350)SEA FILE=DRUGU ABB=ON  INTERFERON#
L178(      5015)SEA FILE=DRUGU ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
               POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L179(      5393)SEA FILE=DRUGU ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L180(        50)SEA FILE=DRUGU ABB=ON  L177 (3A) (L178 OR L179)
L181(         0)SEA FILE=DRUGU ABB=ON  215647-85-1
L182(        59)SEA FILE=DRUGU ABB=ON  L176 OR L180 OR L181
L183          0 SEA FILE=DRUGU ABB=ON  L175 AND L182



L184(        23)SEA FILE=DRUGU ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
               PEGINTRON OR PEG-INTRON OR SCH 54031
L185(     22350)SEA FILE=DRUGU ABB=ON  INTERFERON#
L186(      5015)SEA FILE=DRUGU ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
               POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L187(      5393)SEA FILE=DRUGU ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L188(        50)SEA FILE=DRUGU ABB=ON  L185 (3A) (L186 OR L187)
L189(         0)SEA FILE=DRUGU ABB=ON  215647-85-1
L190(        59)SEA FILE=DRUGU ABB=ON  L184 OR L188 OR L189
L191(     66958)SEA FILE=DRUGU ABB=ON  CHEMOTHERAP? OR ANTITUMOR OR ANTINEOPLAS
               TIC OR ANAPLASTIC OR ONCOLOGY
L192(    142979)SEA FILE=DRUGU ABB=ON  CANCER# OR TUMOR# OR MEOPLASM# OR
               CARCINOMA# OR ASTROCYTOMA#
L193(         9)SEA FILE=DRUGU ABB=ON  L190 AND (L191 OR L192)
L194(     32143)SEA FILE=DRUGU ABB=ON  (HCV OR PEG-DRUGS OR IN VITRO)/TI
L195          6 SEA FILE=DRUGU ABB=ON  L193 NOT L194



L247          6 L183 OR L195

=> file drugnl; d que l206

FILE 'DRUGNL' ENTERED AT 18:11:55 ON 22 JAN 2002
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FILE COVERS 1991 TO 18 Jan 2002 (20020118/ED)

 ###################################################################
 #                                                                 #
 #                    !!! ATTENTION !!!                            #
 #                                                                 #
 #  Welcome to DRUGNL.. This is the Drug News file from            #
 #  IMSworld Publications.                                         #
 #                                                                 #
 #  For detailed information regarding the printed version         #
 #  of this file, please contact IMS HEALTH Customer Services      #
 #  directly by phone at +44(0)20-7393-5888, or email              #
 #  globaldirect@uk.imshealth.com.                                 #
 #                                                                 #
 #  See HELP SUBSCRIPTION for more information.                    #
 ###################################################################
```

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L196(        24)SEA FILE=DRUGNL ABB=ON  TEMOLOZOMID## OR TEMOLDAL# OR TEMODAR
                OR METHAZOLASTON##
L197(        24)SEA FILE=DRUGNL ABB=ON  CCRG 81045 OR ("M AND B" OR MB) (W)
                39831 OR NSC 362856 OR SCH 52365
L198(        24)SEA FILE=DRUGNL ABB=ON  85622-93-1
L199(        24)SEA FILE=DRUGNL ABB=ON  L196 OR L197 OR L198
L200(        43)SEA FILE=DRUGNL ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
                PEGINTRON OR PEG-INTRON OR SCH 54031
L201(      1295)SEA FILE=DRUGNL ABB=ON  INTERFERON#
L202(       147)SEA FILE=DRUGNL ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
                POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L203(        43)SEA FILE=DRUGNL ABB=ON  L200 AND (L201 OR L202)
L204(         0)SEA FILE=DRUGNL ABB=ON  215647-85-1
L205(        43)SEA FILE=DRUGNL ABB=ON  L200 OR L203 OR L204
L206          0 SEA FILE=DRUGNL ABB=ON  L199 AND L205
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CBNB ≡ Chemical Business News Base

```
=> file cbnb; d que l217

FILE 'CBNB' ENTERED AT 18:12:07 ON 22 JAN 2002
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FILE LAST UPDATED: 21 JAN 2002      <20020121/UP>
FILE COVERS 1984 TO DATE.

L207(         9)SEA FILE=CBNB ABB=ON  TEMOLOZOMID## OR TEMOLDAL# OR TEMODAR OR
                METHAZOLASTON##
L208(         0)SEA FILE=CBNB ABB=ON  CCRG 81045 OR ("M AND B" OR MB) (W)
                39831 OR NSC 362856 OR SCH 52365
L209(        33)SEA FILE=CBNB ABB=ON  85622-93-1
L210(        39)SEA FILE=CBNB ABB=ON  L207 OR L208 OR L209
L211(       124)SEA FILE=CBNB ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
                PEGINTRON OR PEG-INTRON OR SCH 54031
L212(      2507)SEA FILE=CBNB ABB=ON  INTERFERON#
L213(       249)SEA FILE=CBNB ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
                POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L214(       105)SEA FILE=CBNB ABB=ON  L211 AND (L212 OR L213)
L215(         0)SEA FILE=CBNB ABB=ON  215647-85-1
L216(       124)SEA FILE=CBNB ABB=ON  L211 OR L214 OR L215
L217          5 SEA FILE=CBNB ABB=ON  L210 AND L216
```

CIN ≡ Chemical Industry Notes

```
=> file cin; d que l228

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FILE COVERS 1974 - 18 JAN 2002 (20020118/ED)  VOL 31  ISS 4
```

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L218(          4)SEA FILE=CIN ABB=ON  TEMOLOZOMID## OR TEMOLDAL# OR TEMODAR OR
                 METHAZOLASTON##
L219(          0)SEA FILE=CIN ABB=ON  CCRG 81045 OR ("M AND B" OR MB) (W) 39831
                 OR NSC 362856 OR SCH 52365
L220(         24)SEA FILE=CIN ABB=ON  85622-93-1
L221(         24)SEA FILE=CIN ABB=ON  L218 OR L219 OR L220
L222(         83)SEA FILE=CIN ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
                 PEGINTRON OR PEG-INTRON OR SCH 54031
L223(       2055)SEA FILE=CIN ABB=ON  INTERFERON#
L224(        445)SEA FILE=CIN ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
                 POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L225(         62)SEA FILE=CIN ABB=ON  L222 AND (L223 OR L224)
L226(          0)SEA FILE=CIN ABB=ON  215647-85-1
L227(         83)SEA FILE=CIN ABB=ON  L222 OR L225 OR L226
L228           0 SEA FILE=CIN ABB=ON  L221 AND L227
```

Prompt ≡ Predicasts Overview of Markets and Technolog

```
=> file promt; d que l240

FILE 'PROMT' ENTERED AT 18:15:04 ON 22 JAN 2002
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 FILE COVERS 1978 TO 19 JAN 2002 (20020119/ED)

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 substance identification.


L229(         52)SEA FILE=PROMT ABB=ON  TEMOLOZOMID## OR TEMOLDAL# OR TEMODAR
                 OR METHAZOLASTON##
L230(         17)SEA FILE=PROMT ABB=ON  CCRG 81045 OR ("M AND B" OR MB) (W)
                 39831 OR NSC 362856 OR SCH 52365
L231(         37)SEA FILE=PROMT ABB=ON  85622-93-1
L232(         72)SEA FILE=PROMT ABB=ON  L229 OR L230 OR L231
L233(        306)SEA FILE=PROMT ABB=ON  PEGINTERFERON OR PEG-INTERFERON OR
                 PEGINTRON OR PEG-INTRON OR SCH 54031
L234(      10196)SEA FILE=PROMT ABB=ON  INTERFERON#
L235(       1404)SEA FILE=PROMT ABB=ON  PEGYLAT? OR POLYETHYLENEGLYCOL OR
                 POLYETHYLEN# GLYCOL OR POLY ETHYLEN# GLYCOL
L236(      10359)SEA FILE=PROMT ABB=ON  MACROGOL# OR CARBOWAX OR PEG#
L237(        236)SEA FILE=PROMT ABB=ON  L234 (3A) (L235 OR L236)
L238(          0)SEA FILE=PROMT ABB=ON  215647-85-1
L239(        404)SEA FILE=PROMT ABB=ON  L233 OR L237 OR L238
L240          13 SEA FILE=PROMT ABB=ON  L232 AND L239
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=> dup rem l241 l242 l243 l244 l245 l246 l247 l206 l217 l228 l240

L206 HAS NO ANSWERS
L228 HAS NO ANSWERS

FILE 'MEDLINE' ENTERED AT 18:18:52 ON 22 JAN 2002

FILE 'CANCERLIT' ENTERED AT 18:18:52 ON 22 JAN 2002

FILE 'CAPLUS' ENTERED AT 18:18:52 ON 22 JAN 2002
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FILE 'BIOTECHNO' ENTERED AT 18:18:52 ON 22 JAN 2002
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FILE 'DRUGU' ENTERED AT 18:18:52 ON 22 JAN 2002
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FILE 'CBNB' ENTERED AT 18:18:52 ON 22 JAN 2002
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FILE 'PROMT' ENTERED AT 18:18:52 ON 22 JAN 2002
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PROCESSING COMPLETED FOR L241
PROCESSING COMPLETED FOR L242
PROCESSING COMPLETED FOR L243
PROCESSING COMPLETED FOR L244
PROCESSING COMPLETED FOR L245
PROCESSING COMPLETED FOR L246
PROCESSING COMPLETED FOR L247
PROCESSING COMPLETED FOR L206
PROCESSING COMPLETED FOR L217
PROCESSING COMPLETED FOR L228
PROCESSING COMPLETED FOR L240

L248 70 DUP REM L241 L242 L243 L244 L245 L246 L247 L206 L217. (19 DUPLICATES REMOVED)

=> file medline cancerlit caplus biosis biotechno embase drugu cbnb promt

FILE 'MEDLINE' ENTERED AT 18:23:59 ON 22 JAN 2002

FILE 'CANCERLIT' ENTERED AT 18:23:59 ON 22 JAN 2002

FILE 'CAPLUS' ENTERED AT 18:23:59 ON 22 JAN 2002
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FILE 'BIOSIS' ENTERED AT 18:23:59 ON 22 JAN 2002

FILE 'BIOTECHNO' ENTERED AT 18:23:59 ON 22 JAN 2002

FILE 'EMBASE' ENTERED AT 18:23:59 ON 22 JAN 2002

FILE 'DRUGU' ENTERED AT 18:23:59 ON 22 JAN 2002

FILE 'CBNB' ENTERED AT 18:23:59 ON 22 JAN 2002

FILE 'PROMT' ENTERED AT 18:23:59 ON 22 JAN 2002

=> d ibib ab 1-70

L248 ANSWER 1 OF 70 CBNB COPYRIGHT 2002 EI
ACCESSION NUMBER: 17(26):36335 CBNB
TITLE: Schering-Plough reviews pharmaceutical research and business progress.
SOURCE: (28 Jun 2001) (900 plus words)
Availability: Schering-Plough Corp, One Giralda Farms, Madison, NJ 07940-1010, USA, Tel: +1 973 822 7000, Fax: +1 973 822 7048, Website: http://www.schering-plough.com
DOCUMENT TYPE: Press Release; (Overview)
LANGUAGE: English
AB Richard Jay Kogan, chairman and chief executive officer of Schering-Plough Corp reviewed highlights of the company's pharmaceutical business and research progress, and discussed efforts to address ongoing manufacturing issues at a meeting with analysts and portfolio managers. In reviewing the company's business operations and research activities, Kogan said that pharmaceuticals make up 85% of total sales, with the largest product groups being allergy/respiratory, anti-infective/anticancer and cardiovascular. The company's animal health and consumer product lines represent about 15% of total sales. Schering-Plough's largest therapeutic category is allergy/respiratory, led by the non-sedating antihistamine Claritin (loratadine), the world's largest- selling antihistamine. Sales increased to $3 bn in 2000, reflecting growth in world allergy markets. Kogan cited one of two partnerships with Merck & Co Inc announced in May 2000, developing a once-daily, fixed-combination tablet containing Schering-Plough's Claritin and Merck's Singulair (montelukast sodium) for the treatment of

allergic rhinitis. The combination therapy has the potential to compete in a US allergy market valued at more than $5 bn. Kogan also highlighted Nasonex (mometasone furoate monohydrate), a potent, once-daily nasal spray for allergies. With worldwide sales up 60% in 2000 to $415 M, Nasonex has captured the No 2 position in the world nasal-inhaled steroid market. Asmanex (mometasone furoate), a next-generation inhaled steroid for asthma, also "would mark the first time a product in this therapeutic class to market on a worldwide basis." The company plans to launch the product on a global basis. In the anti-infective/anticancer area, Kogan reviewed positive developments for the company's **interferon** franchise, including the anticancer/antiviral agent Intron A (**interferon** alfa-2b, recombinant); Rebetron Combination Therapy, containing Rebetol (ribavirin) Capsules and Intron A Injection; and **Peg-Intron** (**peginterferon** alfa-2b), a longer-acting form of Intron A and the world's first **pegylated interferon** on the market. In antiinfective/anticancer category, Kogan highlighted Remicade (infliximab), an anti- inflammatory marketed internationally for the treatment of Crohn's disease and rheumatoid arthritis, which has the potential to be a major factor in what may become a billion-dollar market in Europe; Tequin (gatifloxacin), a new broad- spectrum antibiotic for respiratory infections co-promoted in the US with Bristol-Myers Squibb; **Temodar** (temozolomide), an oral agent approved in the European Union and US for treating certain types of brain cancer; and Caelyx, a long-circulating form of doxorubicin, approved to treat advanced ovarian cancer in fall 2000 in the European Union and in 2001 in Canada. Kogan also reviewed research efforts in the anticancer area, including a farnesyl protein transferase inhibitor in Phase II studies for treating various solid tumours. In cardiovasculars, he discussed Integrilin (eptifibatide), a platelet aggregation inhibitor for cardiovascular patients with certain acute coronary syndromes and those undergoing percutaneous coronary intervention. Ezetimibe forms the basis of the company's cholesterol-management partnership with Merck to develop and market in the US the compound three ways: as a once-daily monotherapy; co- administered with other statins; and as a once-daily, fixed combination tablet with Zocor (simvastatin), Merck's cholesterol-management medicine. With 2000 R&D spending of $1.3 bn, Kogan projected that 2001 R&D expenditures would be around $1.4 bn.

L248 ANSWER 2 OF 70 CBNB COPYRIGHT 2002 EI
ACCESSION NUMBER: 18(1):448 CBNB
TITLE: Schering-Plough projects 2001 and 2002 earnings, highlights business progress, strong products pipeline.
SOURCE: (21 Dec 2001), (900 plus words)
Availability: Schering-Plough Corp, One Giralda Farms, Madison, NJ 07940-1010, USA, Tel: +1 973 822 7000, Fax: +1 973 822 7048, Website: http://www.schering-plough.com
DOCUMENT TYPE: Press Release; (Overview)
LANGUAGE: English

AB Schering-Plough Corp reported projected financial results for 2001 and 2002. Schering-Plough has also completed major structural and organizational changes, forming a new Worldwide Quality Operations unit and strengthening core teams by recruiting very capable and experienced people from inside and outside the company. In 2001, Schering-Plough gained marketing approvals and launched both in the US and the European Union for Clarinex and for **Peg-Intron** for treating chronic hepatitis C. In addition, Rebetol was recently launched in Japan for use only in combination with Intron A for the treatment of chronic hepatitis C. Phase III clinical studies with **Peg-Intron**

are ongoing in Japan. In the US, post-marketing studies with **Peg -Intron** and Rebetol are ongoing to better define optimal treatment regimens using these therapies and further explore their use in treating specific patient populations. Among these is the largest prospective hepatitis C study undertaken to date, which is expected to enrol more than 4000 US patients. The products in Schering-Plough's research pipeline includes: Zetia (ezetimibe); Asmanex (mometasone furoate) and Noxafil (posaconazole). Several promising compounds discovered by Schering-Plough Research Institute include: farnesyl protein transferase (FPT) inhibitor for treating cancer; orally available CCR5 receptor antagonist for treating HIV infection; orally available enzyme inhibitors to combat the hepatitis C virus. Schering-Plough Research Institute is also exploring new market opportunities for existing products. **Peg-Intron** is in Phase III development for two cancer indications, chronic myelogenous leukaemia and malignant melanoma. Remicade (infliximab) is currently in Phase III studies for treating early rheumatoid arthritis and in Phase II studies for treating a debilitating form of spinal rheumatoid arthritis. Also in Phase III clinical development is Caelyx (**pegylated** liposomal doxorubicin hydrochloride) for treating breast cancer. In Phase II clinical studies is Integrilin (eptifibatide) for acute myocardial infarction. **Temodar** (temozolomide), approved for treating certain types of brain cancer, is in Phase II studies for treating a variety of solid tumours. Schering-Plough Corp is a research-based company engaged in the discovery, development, manufacturing and marketing of pharmaceutical products worldwide.

L248 ANSWER 3 OF 70 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:494281 PROMT — print out for "key words in context" for PROMPT hits starts on p. 54.
TITLE: Schering-Plough Reviews Pharmaceutical Research and Business Progress.
SOURCE: PR Newswire, (28 Jun 2001) pp. 4844.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 2451
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB NEW YORK, June 28 /PRNewswire/ --
THIS IS THE FULL TEXT: COPYRIGHT 2001 PR Newswire Association, Inc.

L248 ANSWER 4 OF 70 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:779169 PROMT
TITLE: Sales flat at Schering-Plough as manufacturing problems persist.
SOURCE: Marketletter, (29 Oct 2001)
ISSN: 0951-3175.
PUBLISHER: Marketletter Publications Ltd.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 208
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB Schering-Plough has reported flat third-quarter 2001 sales at $2.38 billion (up 2% excluding currency factors), while net income reached $601 million, or $0.41 per share, an increase of 3% compared with the like, year-earlier period.
THIS IS THE FULL TEXT: COPYRIGHT 2001 Marketletter Publications Ltd.

Subscription: 499.00 British pounds per year. Published weekly. 54-55

Searched by Thom Larson, STIC, 308-7309

Wilton Road, London SW1V 1DE., United Kingdom

L248 ANSWER 5 OF 70 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:555573 PROMT
TITLE: Schering-Plough Reports Sales, Earnings for 2001 Second Quarter, First Half.
SOURCE: PR Newswire, (25 Jul 2001) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 2135
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB 2001 Second Quarter Diluted Earnings Per Share 43 Cents
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L248 ANSWER 6 OF 70 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:560634 PROMT
TITLE: Flat 2nd-qtr sales/EPS at Schering-Plough. (Brief Article)
SOURCE: Marketletter, (30 Jul 2001) .
ISSN: 0951-3175.
PUBLISHER: Marketletter Publications Ltd.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 244
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB Despite strong growth for some of its newer products, Schering-Plough reported flat first-quarter 2001 sales at $2.6 billion (up 3% excluding currency factors) and earnings per share unchanged at $0.43 on net profit of $634 million. International pharmaceutical sales grew 6% (or 13% excluding currency) to $833 million, while domestic turnover declined 6%.
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L248 ANSWER 7 OF 70 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:767772 PROMT
TITLE: Schering-Plough Reports Sales, Earnings for 2001 Third Quarter, First Nine Months.
SOURCE: PR Newswire, (23 Oct 2001) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 2041
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB 2001 Third Quarter Diluted Earnings Per Share up 3 Percent to 41 Cents
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L248 ANSWER 8 OF 70 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:308802 PROMT
TITLE: Manufacturing woes hit Schering-Plough.
SOURCE: Marketletter, (23 Apr 2001) .
ISSN: 0951-3175.
PUBLISHER: Marketletter Publications Ltd.
DOCUMENT TYPE: Newsletter
LANGUAGE: English

WORD COUNT: 290
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB Fulfiling its profit warning earlier this year, Schering-Plough has reported first-quarter 2001 diluted earnings per share down 10% at $0.38 on net income of $564 million, compared with $628 million in the like, 2000 period, as it tries to deal with manufacturing plant problems cited by the US Food and Drug Administration (Marketletters passim).
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Subscription: 499.00 British pounds per year. Published weekly. 54-55 Wilton Road, London SW1V 1DE., United Kingdom

L248 ANSWER 9 OF 70 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:916534 PROMT
TITLE: Schering-Plough Projects 2001 and 2002 Earnings, Highlights Business Progress, Strong Product Pipeline.
SOURCE: PR Newswire, (21 Dec 2001) pp. NYF07121122001.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 2316
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB KENILWORTH, N.J. -- Schering-Plough Corporation today reported projected financial results for 2001 and 2002 in conjunction with its announcement that the U.S. Food and Drug Administration (FDA) has granted marketing approval for CLARINEX(R) (desloratadine) 5 mg Tablets for the treatment of seasonal allergic rhinitis (SAR) in adults and children 12 years of age and older, and that the company is in negotiations with FDA to reach a consent decree to resolve issues involving the company's compliance with current Good Manufacturing Practices (GMPs) at manufacturing facilities in New Jersey and Puerto Rico. Terms of the consent decree under negotiation include a possible payment by Schering-Plough to the federal government that may be as high as $500 million, subject to resolution of other terms of the final agreement. (See separate Schering-Plough press releases.)
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L248 ANSWER 10 OF 70 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:297991 PROMT
TITLE: Schering-Plough Reports Sales, Earnings for 2001 First Quarter.
SOURCE: PR Newswire, (17 Apr 2001) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 1577
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB 2001 First Quarter Diluted Earnings Per Share Down 10% to 38 cents
THIS IS THE FULL TEXT: COPYRIGHT 2001 PR Newswire Association, Inc.

L248 ANSWER 11 OF 70 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:66246 PROMT
TITLE: Schering-Plough Reports Sales, Earnings for 2000 Fourth Quarter and Full Year.
SOURCE: PR Newswire, (25 Jan 2001) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter

LANGUAGE: English
WORD COUNT: 1905
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB 2000 Fourth Quarter Diluted Earnings Per Share Up 15% to 39 Cents; THIS IS THE FULL TEXT: COPYRIGHT 2001 PR Newswire Association, Inc.

L248 ANSWER 12 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:747647 CAPLUS
DOCUMENT NUMBER: 135:308875
TITLE: Drugs retained in target tissue over long time
INVENTOR(S): Sato, Haruya; Hayashi, Eiko; Shirae, Hideyuki
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074399	A1	20011011	WO 2001-JP2604	20010328

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2000-93775 A 20000330
AB Disclosed are a ligand attached to a polyethylene glycol wherein a polyethylene glycol chain is attached to a ligand having a binding affinity to a specific receptor or a protein (antigen, etc.) located on the cell membrane of a target tissue and being capable of avoiding the incorporation into cells; and medicines wherein a drug (a physiol. active substance, etc.) is attached to this polyethylene glycol chain. Thus, a novel ligand, which can be accumulated at a high concn. around a target tissue and has good retention properties in the blood, and excellent medicines, wherein a drug (a physiol. active substance, etc.) efficacious in the above target tissue is attached thereto, can be provided. (Gal)3-**polyethylene glycol-interferon**-.alpha. conjugate was prepd. and administered to mice; higher concns. of interferons were detd. in the plasma and liver tissues, as compared to the ones obtained by administration of unmodified interferons.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L248 ANSWER 13 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:545514 CAPLUS
DOCUMENT NUMBER: 135:102555
TITLE: Combination of temozolomide and **PEGylated interferon**-.alpha. for treating **cancer**
INVENTOR(S): **Zaknoen, Sara L.**
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052882	A1	20010726	WO 2001-US2374	20010122

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-177624 P 20000124

AB A method for treating a human patient afflicted with **cancer** is provided in which therapeutically effective amts. of temozolomide and **PEGylated interferon**-.alpha. are administered. Also provided is a medical kit comprising: (a) a supply of temozolomide; (b) a supply of **PEGylated interferon**-.alpha.; and (c) printed instructions for administering temozolomide and **PEGylated interferon**-.alpha. to a **cancer** patient.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L248 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:265599 CAPLUS
DOCUMENT NUMBER: 134:294522
TITLE: Interferon .alpha. homologues
INVENTOR(S): Heinrichs, Volker; Chen, Teddy; Patten, Phillip A.
PATENT ASSIGNEE(S): Maxygen, Inc., USA
SOURCE: PCT Int. Appl., 209 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001025438	A2	20010412	WO 2000-US27781	20001006

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-415183 A 19991007

AB .alpha. Interferon homologues (both nucleic acids and polypeptides) are provided. Compns. including these interferon homolog polypeptides and nucleic acids, recombinant cells comprising said homolog polypeptides and nucleic acids, methods of making the new homologues, antibodies to the new homologues, and methods of using the homologues are provided. Integrated systems comprising the sequences of the nucleic acids or polypeptides are also provided. These interferon .alpha. homologues are useful for inhibiting **tumor** growth and viral replication, and are also

useful for treating autoimmune diseases.

L248 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:817201 CAPLUS
DOCUMENT NUMBER: 135:343312
TITLE: Melanoma therapy using **pegylated interferon**-.alpha.
INVENTOR(S): Rybak, Mary Ellen; Rose, Esther Helen
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 7 pp., Cont. of U.S. Ser. No. 545,312.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001038833	A1	20011108	US 2001-904263	20010712

PRIORITY APPLN. INFO.: US 1999-128308 P 19990408
US 2000-545312 A1 20000407

AB Methods for treating treatment-naive as well as treatment-experienced patients having melanoma to increase the progression-free survival time involving administering a therapeutically effective amt. of **pegylated interferon**-.alpha. as adjuvant therapy to definitive surgery are disclosed. The **pegylated interferon**-.alpha. is either **pegylated interferon**-.alpha.2a or **pegylated interferon** -.alpha.2b.

L248 ANSWER 16 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:924286 CAPLUS
DOCUMENT NUMBER: 136:36372
TITLE: Renal cell **carcinoma** treatment
INVENTOR(S): Rybak, Mary Ellen; Rose, Esther Helen
PATENT ASSIGNEE(S): Rybak, Mary, USA
SOURCE: U.S. Pat. Appl. Publ., 6 pp., Division of U.S. Ser. No. 544,232.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001053548	A1	20011220	US 2001-901522	20010709

PRIORITY APPLN. INFO.: US 1999-128295 P 19990408
US 2000-544232 A3 20000407

AB Methods for treating treatment-naive as well as treatment-experienced patients having RCC to achieve at least a partial **tumor** response involving administering a therapeutically effective amt. of **pegylated interferon**-alpha, e.g., **pegylated interferon** alpha-2b as monotherapy or in assocn. with a therapeutically effective amt. of IL-2 are disclosed.

L248 ANSWER 17 OF 70 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001492848 MEDLINE
DOCUMENT NUMBER: 21426507 PubMed ID: 11535501

TITLE: Phase 1 study of **polyethylene glycol** formulation of **interferon** alpha-2B (Schering 54031) in Philadelphia chromosome-positive chronic myelogenous leukemia.
AUTHOR: Talpaz M; O'Brien S; Rose E; Gupta S; Shan J; Cortes J; Giles F J; Faderl S; Kantarjian H M
CORPORATE SOURCE: Department of Bioimmunotherapy, M. D. Anderson Cancer Center, Houston, TX, USA.
SOURCE: BLOOD, (2001 Sep 15) 98 (6) 1708-13.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010906
Last Updated on STN: 20011015
Entered Medline: 20011011

AB Interferon alpha (IFN-alpha) therapy improves prognosis in Philadelphia chromosome (Ph)-positive chronic myelogenous leukemia (CML). Polyethylene glycol (PEG) attached to IFN-alpha prolongs its half-life and may offer better therapy. The aims of this phase 1 study were to define the maximal tolerated dose (MTD), dose-limiting toxicities (DLTs), and response with PEG IFN-alpha-2b. Twenty-seven adults with Ph(+) CML in chronic or accelerated phases, in whom IFN-alpha treatment had failed, were studied. Patients had hematologic (9 patients) or cytogenetic resistance (12 patients) or intolerance to IFN-alpha (6 patients). PEG IFN-alpha-2b was given as a weekly subcutaneous injection starting at 0.75 microg/kg weekly and escalating to 1.5, 3, 4.5, 6, 7.5, and 9.0 microg/kg. The MTD was defined at 7.5 to 9 microg/kg; DLT included severe fatigue, neurotoxicity, liver function abnormalities, and myelosuppression. Longer administration of PEG IFN-alpha-2b resulted in chronic side effects not observed earlier, which defined the MTD and DLT. The proposed phase 2 dose of PEG IFN-alpha-2b was 6 microg/kg weekly. Among 19 patients with active disease, 7 (37%) achieved complete hematologic response (CHR); 2 (11%) had a cytogenetic response (complete). Among 8 patients treated in CHR, 7 (87%) improved cytogenetic response to complete (4 patients) or partial (3 patients). All 6 patients intolerant to IFN-alpha tolerated PEG IFN-alpha-2b; 4 improved their cytogenetic response. The results show that PEG IFN-alpha-2b is easier to deliver (once weekly), better tolerated, and perhaps more effective than IFN-alpha.

L248 ANSWER 18 OF 70 MEDLINE
ACCESSION NUMBER: 2001448919 MEDLINE
DOCUMENT NUMBER: 21386658 PubMed ID: 11494553
TITLE: Present status of clinical trials on long-acting IFNs preparations (PEG-IFN alpha 2a, alpha 2b, IFN alpha-minipellet).
AUTHOR: Tanikawa K
CORPORATE SOURCE: International Institute for Liver Research.
SOURCE: NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (2001 Jul) 59 (7) 1369-73. Ref: 6
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20020121
Entered Medline: 20011204

AB Interferon(IFN) is an essential component of the treatment of chronic HCV infection and at present, it is the most important to improve its efficacy, not only for HCV chronic liver diseases, but also for the prevention of HCV-associated hepatocellular **carcinoma**. Two long-acting IFN preparations(PEG-IFN alpha 2a and 2b) have been used at present and clinical studies have shown that sustained virologic, biochemical and histological responder rates are significantly higher in PEG-IFN-treated patients with HCV associated chronic hepatitis and cirrhosis comparing with ones treated with conventional IFN. In addition, PEG-IFN treatment in combination with ribavirin seems to be the best for HCV-associated chronic liver diseases.

L248 ANSWER 19 OF 70 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001184570 MEDLINE
DOCUMENT NUMBER: 21142859 PubMed ID: 11230473
TITLE: Phase I trial of 40-kd branched **pegylated interferon** alfa-2a for patients with advanced renal cell **carcinoma**.
AUTHOR: Motzer R J; Rakhit A; Ginsberg M; Rittweger K; Vuky J; Yu R; Fettner S; Hooftman L
CORPORATE SOURCE: Genitourinary Oncology Service, Division of Solid Tumor Oncology, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.
SOURCE: JOURNAL OF CLINICAL ONCOLOGY, (2001 Mar 1) 19 (5) 1312-9. Journal code: JCO; 8309333. ISSN: 0732-183X.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010329

AB PURPOSE: **Pegylated** (40 kd) **interferon** alfa-2a (IFNalpha2a) (PEGASYS, Hoffman-La Roche, Nutley, NJ; PEG-IFN) is a modified form of recombinant human IFNalpha2a with sustained absorption and prolonged half-life after subcutaneous administration. A phase I study of PEG-IFN with pharmacokinetic and pharmacodynamic evaluations was conducted in previously untreated patients with advanced renal cell **carcinoma** (RCC). PATIENTS AND METHODS: Twenty-seven patients were enrolled onto cohorts of three or six patients. PEG-IFN was administered on a weekly basis by subcutaneous injection. The dose was escalated from 180 microg/wk to a maximum of 540 microg/wk in 90-microg increments. Serial venous blood samples were drawn to assess concentrations of PEG-IFN and two immunologic surrogates, neopterin and 2'-5' oligoadenylate synthetase (OAS). RESULTS: The maximum-tolerated dose was determined as 540 microg/wk, because two patients experienced dose-limiting toxicity within 28 days of starting treatment. One developed serum grade 3 ALT elevation, and a second developed grade 3 fatigue. Six patients were treated at 450 microg/wk without dose-limiting toxicity. Over the course of treatment, the side-effect profile was mostly mild to moderate in intensity. Adverse events included fatigue, fever, headache, myalgia, nausea, and decreased appetite. Five patients (19%) achieved a partial

response. The mean maximum serum concentration increased from 5.0 to 27 ng/mL, and mean area under the curve increased from 247 to 2,981 ng/h/mL, with dose escalation from 180 microg/wk to 540 microg/wk. Serum concentration of PEG-IFN was sustained at close to peak during the dosing interval, and steady-state was achieved in approximately 5 weeks. The immunologic surrogates, neopterin and OAS, were induced at all doses with a sustained concentration profile similar to PEG-IFN. CONCLUSION: PEG-IFN is a modified form of IFNalpha2a with distinct pharmacokinetic advantages and immunomodulatory and **antitumor** activity for patients with advanced RCC. A dose of 450 microg/wk by subcutaneous administration was determined as a suitable dose for further study. PEG-IFN is more convenient to administer than IFNalpha and has potential for increased efficacy, less toxicity, or both. The efficacy and toxicity of PEG-IFN will be further assessed in clinical trials and compared with IFNalpha.

L248 ANSWER 20 OF 70 MEDLINE
ACCESSION NUMBER: 2001448897 MEDLINE
DOCUMENT NUMBER: 21386636 PubMed ID: 11494531
TITLE: Recent progress and prospective view of chronic hepatitis C research.
AUTHOR: Otsuka M; Kato N; Omata M
CORPORATE SOURCE: Department of Gastroenterology, Faculty of Medicine, University of Tokyo.
SOURCE: NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (2001 Jul) 59 (7) 1243-7. Ref: 20
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20020121
Entered Medline: 20011204

AB Hepatitis C is a major public health problem because of the high incidence of its related hepatocellular **carcinoma**. With the progress in molecular biology, the mechanisms of persistent infection, chronic inflammation, and hepatocarcinogenesis have been described in terms of virus, host, and virus-cell interactions. On the other hand, clinically, some recent studies using a large number of subjects with long-term observation after interferon therapy showed that improving hepatic inflammation might be associated with regression or retardation of fibrosis. However, current therapy for hepatitis C, although effective in some patients, is problematic even though the efficacy of combination therapy, **interferon** plus ribavirin, or **PEG-interferon** has been reported. Here we review the progress and discuss the prospective view of hepatitis C virus research from a point of view of both basic and clinical aspects.

L248 ANSWER 21 OF 70 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 2001:33151039 BIOTECHNO
TITLE: **Cancer chemotherapy**: Teaching old drugs new tricks
AUTHOR: Kane B.
SOURCE: Annals of Internal Medicine, (18 DEC 2001), 135/12 (1107-1110)
CODEN: AIMEAS ISSN: 0003-4819
DOCUMENT TYPE: Journal; General Review

Searched by Thom Larson, STIC, 308-7309

COUNTRY: United States
LANGUAGE: English

L248 ANSWER 22 OF 70 MEDLINE
ACCESSION NUMBER: 2001264650 MEDLINE
DOCUMENT NUMBER: 21255945 PubMed ID: 11356929
TITLE: Improved pharmacokinetic properties of a **polyethylene glycol**-modified form of **interferon**-beta-1a with preserved in vitro bioactivity.
AUTHOR: Pepinsky R B; LePage D J; Gill A; Chakraborty A; Vaidyanathan S; Green M; Baker D P; Whalley E; Hochman P S; Martin P
CORPORATE SOURCE: Biogen, Inc., Cambridge, Massachusetts, USA.. Blake_Pepinsky@biogen.com
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (2001 Jun) 297 (3) 1059-66.
Journal code: JP3; 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010618
Last Updated on STN: 20010618
Entered Medline: 20010614

AB Interferon therapies suffer from a relatively short half-life of the products in circulation. To address this issue we investigated the effects of polyethylene glycol modification (PEGylation) on the pharmacokinetic properties of human **interferon** (IFN)-beta-1a. **PEGylation** with a linear 20-kDa PEG targeted at a single site on the N-terminal amine had no deleterious effect on its specific activity in an in vitro antiviral assay. In monkeys, PEG IFN-beta-1a treatment induced neopterin and beta2-microglobulin expression (pharmacodynamic markers of activity). Systemic clearance values in monkeys, rats, and mice decreased, respectively, from 232, 261, and 247 ml/h/kg for the unmodified IFN-beta-1a to 30.5, 19.2, and 18.7 ml/h/kg for the PEGylated form, while volume of distribution values decreased from 427, 280, and 328 ml/kg to 284, 173, and 150 ml/kg. The decreased clearance and volume of distribution resulted in higher serum antiviral activity in the PEG IFN-beta-1a-treated animals. In the rat, a more extensive set of dosing routes was investigated, including intraperitoneal, intratracheal, and oral administration. Bioavailability for the PEG IFN-beta-1a was similar to the unmodified protein for each of the extravascular routes examined. For the intraperitoneal route, bioavailability was almost 100%, whereas for the oral and intratracheal routes absorption was low (<5%). In rats, subcutaneous bioavailability was moderate (28%), whereas in monkeys it was approximately 100%. In all instances an improved pharmacokinetic profile for the PEGylated IFN-beta-1a was observed. These findings demonstrate that PEGylation greatly alters the pharmacokinetic properties of IFN-beta-1a, resulting in an increase in systemic exposure following diverse routes of administration.

L248 ANSWER 23 OF 70 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001654531 IN-PROCESS
DOCUMENT NUMBER: 21563958 PubMed ID: 11707145
TITLE: Pegylated cytokines: potential application in immunotherapy of **cancer**.
AUTHOR: Eliason J F
CORPORATE SOURCE: Barbara Ann Karmanos Cancer Institute, Wayne State

University, Detroit, Michigan, USA.
SOURCE: BioDrugs, (2001) 15 (11) 705-11.
Journal code: D3A; 9705305. ISSN: 1173-8804.
PUB. COUNTRY: New Zealand
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20011115
Last Updated on STN: 20011115

AB Conjugation of the polymer polyethylene glycol (PEG) to proteins can significantly decrease their clearance from plasma, thus increasing their half-lives in vivo. The increased half-life of PEG-proteins is directly proportional to the total molecular weight of the construct. This approach has been used to design cytokine constructs that can be administered once a week, rather than on a daily or alternate-day schedule. Two cytokines for which this approach appears to be successful are **PEG-interferon**-alpha-2a (**PEG**-IFNalpha-2a) and PEG-granulocyte colony- stimulating factor (PEG-G-CSF). Both use high molecular weight PEG (20 to 40kD) to give sufficiently long duration in vivo. In the case of PEG-G-CSF conjugates, the in vivo efficacy is directly proportional to molecular weight, whereas the in vitro activity is inversely proportional, suggesting that overall duration of contact is more important than the affinity of the interaction. Conjugates of a number of other cytokines have been prepared, but until recently, few have used the high molecular weight polymers. In the future, as this approach is taken to make new PEG-cytokine constructs, thorough pharmacokinetic studies will be essential for their development and clinical use.

L248 ANSWER 24 OF 70 MEDLINE
ACCESSION NUMBER: 2001669678 IN-PROCESS
DOCUMENT NUMBER: 21572761 PubMed ID: 11715332
TITLE: [In Process Citation].
Erkennung und Behandlung der chronischen Hepatitis C. Praktische Empfehlungen und neue Entwicklungen.
AUTHOR: Niederau C
CORPORATE SOURCE: Klinik fur Innere Medizin, St.-Josef-Hospital Oberhausen, Akademisches Lehrkrankenhaus, Universitat Essen..
claus.niederau@uni-duesseldorf.de
SOURCE: MEDIZINISCHE KLINIK, (2001 Oct 15) 96 (10) 599-607.
Journal code: M9K; 8303501. ISSN: 0723-5003.
PUB. COUNTRY: Germany: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20011122
Last Updated on STN: 20011122

AB BACKGROUND: Chronic hepatitis C affects more than 500,000 people in Germany and is one of the most important chronic liver diseases. A large part of liver cirrhosis and **cancer** as well as most liver transplantations are today caused by hepatitis C. METHODS: The review analyzes the recent Medline-literature and own data about diagnosis and therapy of chronic hepatitis C with special emphasis on practical consequences of the new data. RESULTS AND DISCUSSION: In contrast to HBV, hepatitis C is usually not transmitted by sexual and perinatal means which leads to corresponding recommendations by official health care organizations. Diagnosis of chronic hepatitis C with antibody tests and HCV-RNA is today easy and reliable. HCV genotype and quantitative measurements of HCV-RNA should be done prior to antiviral therapy. Liver biopsy is necessary to determine the disease stage and the urgency for antiviral therapy. Young subjects with biochemical and histological

inflammation should be treated. The standard therapy with **pegylated interferon** and ribavirin is able to eliminate HCV-RNA from serum in approximately 60% of the patients. In patients with genotype 1 and high virus load therapy can eliminate HCV-RNA in 30-40% while therapy is successful in > 90% of patients with genotype 3 and low virus load. There is increasing evidence that antiviral therapy causes beneficial effects on disease progression and **cancer** risk also in patients in whom HCV-RNA is not eliminated.

L248 ANSWER 25 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:479028 BIOSIS
DOCUMENT NUMBER: PREV200100479028
TITLE: Optimal biological dose of pegilated **interferon** -alpha (**PEG** IFN-alpha) inhibits angiogenesis and growth of human transitional cell **carcinoma** in the bladder of nude mice.
AUTHOR(S): Kedar, Daniel M. (1); Slaton, Joel W. (1); Dinney, Colin P. N. (1); Killion, Jerald J. (1); Fidler, Isaiah J. (1)
CORPORATE SOURCE: (1) M D Anderson Cancer Center, Houston, TX USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 568. print. Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research New Orleans, LA, USA March 24-28, 2001
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L248 ANSWER 26 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:524361 CAPLUS
TITLE: Status quo ante, and future of polymer drugs
AUTHOR(S): Maeda, Hiroshi
CORPORATE SOURCE: Dep. Microbiology, Kumamoto Univ. Med. Sch., Kumamoto, 860-0811, Japan
SOURCE: Drug Delivery Syst. (2001), 16(3), 136-142
CODEN: DDSYEI; ISSN: 0913-5006
PUBLISHER: Nippon DDS Gakkai Jimukyoku
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Polymeric drugs have been investigated in exptl. as well as clin. settings such as SMIANCS and L-asparaginase since 1970s. Accumulated data show that there are common characteristics among wide range of polymer therapeutics: i.e. prolonged plasma half-life, highly efficient **tumor** targeting capability and EPR (enhanced permeability and retention)effect. The factors involved in EPR effect are common denominators in both **cancer** and inflammation, indicating that EPR effect of polymer drugs can be applicable to infectious and inflammatory diseases in addn. to **cancer**. Remarkable clin. effects of **PEG-interferon** a conjugates and related issues are also described as promising future prospects of polymeric drugs.

L248 ANSWER 27 OF 70 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 2001:32098700 BIOTECHNO
TITLE: Projecting future drug expenditures-2001
AUTHOR: Mehl B.; Santell J.
CORPORATE SOURCE: J. Santell, ASHP Ctr. on Pharm. Practice Mgmt., American Soc. of Hlth.-System Pharm., 7272 Wisconsin Avenue, Bethesda, MD 20814, United States.

SOURCE: American Journal of Health-System Pharmacy, (15 JAN 2001), 58/2 (125-133), 60 reference(s)
CODEN: AHSPEK ISSN: 1079-2082
DOCUMENT TYPE: Journal; General Review
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Drug cost projections for 2001 and factors that are likely to influence drug costs are discussed. The year 2000 introduced many new factors into the decision-making process for drug pricing and raised new considerations regarding drug therapy, distribution, and costs. It is anticipated that drug costs will continue to increase at a rate of 11-15% in 2001. Research and development expenditures for new drugs continue to grow and are estimated to be $26.4 billion in 2000, but the number of new drug approvals, especially for new entities, has not increased significantly. The generic drug industry has been expanding, and sales of generics are expected to increase to $20 billion by 2005. Drug costs also keep rising, and sales may reach $243 billion by 2008; this amounts to 12.6% of total health care spending, compared with 8.1% in 1999. There is a trend toward increasing the rate of conversion of prescription drugs to nonprescription status; this may reduce drug budgets somewhat. 2001 will see new systems of drug distribution and pricing, a federal prospective pricing system for ambulatory care patients covered by Medicare, drug imports from foreign manufacturers, and states taking legal action to reduce prescription drug costs. Drug costs in 2001 are expected to continue to increase at double-digit rates. The increase in costs is due to increased utilization, to new products replacing older products, and to price increases for drugs currently on the market.

L248 ANSWER 28 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:463518 BIOSIS
DOCUMENT NUMBER: PREV200100463518
TITLE: **PEG**-modified **interferon**-alpha (OmniferonTM) with well conserved bioactivity.
AUTHOR(S): Malik, F. (1); Hussain, N.; Maidment, S.; Delgado, C.; Brown, K. E.; Robertson, C. D.; Tomlin, L.; Nicolson, M.; Francis, G. E. (1)
CORPORATE SOURCE: (1) PolyMASC Pharmaceuticals plc, London, NW3 2EZ UK
SOURCE: Experimental Hematology (Charlottesville), (August, 2001) Vol. 29, No. 8 Supplement 1, pp. 45. print.
Meeting Info.: 30th Annual Meeting of the International Society for Experimental Hematology Tokyo, Japan August 25-28, 2001
ISSN: 0301-472X.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L248 ANSWER 29 OF 70 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2001552968 IN-PROCESS
DOCUMENT NUMBER: 21485391 PubMed ID: 11599896
TITLE: The EORTC melanoma group translational research program on prognostic factors and ultrastaging in association with the adjuvant therapy trials in stage II and stage III melanoma. European Organization for Research and Treatment of **Cancer**.
AUTHOR: Eggermont A M; Keilholz U; Testori A; Cook M; Lienard D; Ruiter D J
CORPORATE SOURCE: EORTC-Melanoma Group, Brussels, Belgium.. eggermont@chih.azr.nl

SOURCE: ANNALS OF SURGICAL ONCOLOGY, (2001 Oct) 8 (9 Suppl) 38S-40S.
Journal code: 9420840. ISSN: 1068-9265.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20011016
Last Updated on STN: 20020122

AB Last year the Melanoma Group of the European Organization for Research and Treatment of **Cancer** (EORTC-MG) completed accrual (1418 patients) for trial EORTC 18952, a three-arm phase III trial evaluating adjuvant therapy with two different intermediate doses of interferon (IFN) alfa-2b versus observation for stage IIB-III melanoma. About 25% of the patients entered the trial with **tumor**-positive sentinel nodes (SNs). Prognosis was significantly better in SN-positive patients than in patients with palpable regional node involvement ($P < .00001$). Subsequently the EORTC-MG embarked on two large phase III trials of adjuvant therapy based on the **tumor** status of the SN. In trial EORTC 18961 for stage II melanoma, GM2-KLH/QS-21 vaccination is compared with observation (1300 patients); in trial EORTC 18991 for stage III melanoma, 5-year treatment with **pegylated interferon** alfa-2b (**PEG-Intron**) is compared with observation (900 patients). Translational research projects will compare SN assessment by hematoxylin and eosin (H&E) staining, immunohistochemistry (IHC), and reverse transcriptase-polymerase chain reaction (RT-PCR) to determine the relative accuracy of each method and its correlation to relapse and survival of patients with stage II melanoma. In stage III patients, a similar workup of the most proximal nonsentinel node in the full lymph-node dissection specimen will indicate the accuracy of each methodology to detect nodal metastasis beyond the SN and the prognostic significance thereof. These findings will be correlated to the results of sequential blood testing by RT-PCR and by **tumor** marker assays for S100, TA90, and angiostatin. In addition, **tumor**-positive and **tumor**-negative SNs will be assessed for activated cytotoxic T lymphocytes and downregulation of dendritic cell functions.

L248 ANSWER 30 OF 70 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE

ACCESSION NUMBER: 2001:32816517 BIOTECHNO
TITLE: **Interferon**-alfa - Based treatment of chronic myeloid leukemia and implications of signal transduction inhibition
AUTHOR: Talpaz M.
CORPORATE SOURCE: Dr. M. Talpaz, M.D. Anderson Cancer Center, Box 302, 1515 Holcombe Blvd, Houston, TX 77030, United States.
SOURCE: Seminars in Hematology, (2001), 38/3 SUPPL. 8 (22-27), 15 reference(s)
CODEN: SEHEA3 ISSN: 0037-1963
DOCUMENT TYPE: Journal; General Review
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The cytokine **interferon**-alfa (IFN-.alpha.) has substantial activity in chronic myeloid leukemia (CML) and is the nontransplant standard of care for chronic-phase disease. When used as front-line therapy, IFN-.alpha. induces a state of **tumor** dormancy and delays progression to advanced phase. Unfortunately, IFN-.alpha. is associated with substantial toxicity at therapeutic doses. The introduction of **pegylated** IFN-.alpha. (**PEG** -IFN-.alpha.), a modified form of the protein that permits weekly

administration, may alleviate some of the problems observed with IFN-.alpha.. Combination regimens of IFN-.alpha. with other drugs such as cytarabine (Ara-C) appear to enhance efficacy and are currently under investigation. The tyrosine kinase inhibitor imatinib mesylate (Gleevec.TM., Novartis Pharmaceuticals Corp, East Hanover, NJ) (formerly STI571) also is efficacious in chronic-phase CML, with a low toxicity profile. However, its potential to cure CML remains unknown even though it achieves frequent cytogenetic responses. To enhance treatment outcome, a combination of IFN-.alpha. and imatinib mesylate therapies is proposed. Low-dose IFN-.alpha. may be given after imatinib mesylate-induced remission as a specific immune stimulant to consolidate the remission. Recent data showing a possible additive effect of imatinib mesylate and IFN-.alpha. suggest that concurrent use of these agents may also be more effective than single use, particularly in advanced stages of CML where imatinib mesylate has activity but resistance develops. Copyright .COPYRGT. 2001 W.B. Saunders Company.

L248 ANSWER 31 OF 70 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 2001:32720924 BIOTECHNO
TITLE: First experience with pegylated interferon in practice ERSTE ERFAHRUNGEN MIT PEGYLIERTEM INTERFERON IN DER PRAXIS
AUTHOR: Hein R.
CORPORATE SOURCE: Dr. R. Hein, Klinikum rechts der Isar, Klin./Poliklin. Dermatol./Allergol., Munchen, Germany.
SOURCE: Onkologie Service Aktuell, (2001), -/2 (7-9)
CODEN: OSAKFB ISSN: 0949-3441
DOCUMENT TYPE: Journal; Note
COUNTRY: Germany, Federal Republic of
LANGUAGE: German

L248 ANSWER 32 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:578087 BIOSIS
DOCUMENT NUMBER: PREV200100578087
TITLE: IFN-A2 and PEG-IFN-A2 inhibit **tumor** induced agiogenesis in the murine dermis model.
AUTHOR(S): Bauer, Joseph A.; Grane, Ronald W.; Jacobs, Barbara; Morrison, Bei Hu; Borden, Ernest C.; Lindner, Daniel J.
SOURCE: Journal of Interferon and Cytokine Research, (2001) Vol. 24, No. Supplement 1, pp. S.62. print.
Meeting Info.: Annual Meeting of the International Society for Interferon and Cytokine Research Cleveland,, OH, USA October 07-11, 2001
ISSN: 1079-9907.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L248 ANSWER 33 OF 70 CBNB COPYRIGHT 2002 EI
ACCESSION NUMBER: 17(43):54906 CBNB
TITLE: Schering-Plough reports sales, earnings for 3Q 2001, first nine months. [2 tables]
SOURCE: Schering-Plough announces 3Q and nine months of 2001 results (23 Oct 2001)
Availability: Schering-Plough Corp, One Giralda Farms, Madison, NJ 07940-1010, USA, Tel: +1 973 822 7000, Fax: +1 973 822 7048, Website: http://www.schering-plough.com
DOCUMENT TYPE: Journal; Company Publication
LANGUAGE: English

Searched by Thom Larson, STIC, 308-7309

AB Schering-Plough Corp reported financial results for 3Q and nine months ended Sep 2001. Net income was $601 M for 3Q 2001 (net income of $591 M in 3Q 2000). For 3Q 2001 sales of $2.4 bn were flat compared with 3Q 2000 period. Net income was $1.8 bn for nine months of 2001 (net income of $1.9 bn in nine months of 2000). Sales for nine months of 2001 totalled $7.3 bn ($7.4 bn in nine months of 2000). During 3Q 2001, worldwide pharmaceutical sales increased 1% to $2.1 bn. Some of the products and their sales for 3Q 2001 were: Claritin (loratadine) increased 5% to $828 M; Nasonex (mometasone furoate monohydrate) nasal spray increased 39% to $136 M; Intron A franchise decreased 11% to $301 M (the franchise includes Intron A (**interferon** alfa-2b)); **Peg-Intron** (**peginterferon** alfa-2b), a longer-acting form of Intron A (as monotherapy and, internationally, in combination with Rebetol (ribavirin); and Rebetron combination therapy containing Intron A and Rebetol); **Temodar** (temozolomide) increased 20% to $45 M; Integrilin (eptifibatide) injection increased 14% to $59 M; and that of Remicade (infliximab) went up sharply to $42 M. Animal health products sales totalled $169 M; over-the-counter product sales decreased 26% to $43 M and sun care product sales increased to $11 M for 3Q 2001. During nine months of 2001, worldwide sales of pharmaceuticals decreased 1% to $6.3 bn and that of animal health products decreased 2% to $493 M. Research and development expenses were $310 M during 3Q 2001 ($340 M in 3Q 2000) and $934 M for nine months of 2001 ($975 M in nine months of 2000). Schering-Plough is a research-based company engaged in the discovery, development, manufacturing and marketing of pharmaceutical products worldwide. The unaudited report and net sales of major product for 3Q and nine months ended Sep 2000 and 2001 of Schering-Plough Corp are highlighted in two different tables.

L248 ANSWER 34 OF 70 CBNB COPYRIGHT 2002 EI
ACCESSION NUMBER: 17(16):22033 CBNB
TITLE: Schering-Plough reports sales, earnings for 2001 1Q. [2 tables]
SOURCE: Schering-Plough 1Q 2001 results (17 Apr 2001) Availability: Schering-Plough Corp, One Giralda Farms, Madison, NJ 07940-1010, USA, Tel: +1 973 822 7000, Fax: +1 973 822 7048, Website: http://www.schering-plough.com
DOCUMENT TYPE: Journal; Company Publication
LANGUAGE: English

AB Schering-Plough Corp reported net income of $564 M for 1Q ended Mar 2001 (net income of $628 M in 1Q ended Mar 2000). Sales were $2.3 bn for 1Q 2001 (-3% from $2.4 bn in 1Q 2000). During 1Q 2001, worldwide pharmaceutical sales totalled $1.9 bn. Worldwide sales of the Claritin (loratadine) nonsedating antihistamine line grew 8% to $718 M and that of Nasonex (mometasone furoate monohydrate) Nasal Spray increased 13% to $92 M during 1Q 2001. Combined sales of the anti-infective/anticancer agent Intron A (**interferon** alfa-2b); **Peg-Intron** (**peginterferon** alfa-2b); and Rebetron Combination Therapy containing Intron A and Rebetol (ribavirin, USP) Capsules, totalled $326 M during 1Q 2001. Also contributing to 1Q 2001 worldwide sales were **Temodar** (temozolomide), with sales of $43 M; Integrilin (eptifibatide) Injection, up 38% to $38 M; and Remicade (infliximab), with higher sales of $27 M. US pharmaceutical sales in 1Q 2001 totalled $1.2 bn. In allergy/respiratory, 1Q 2001 US sales of the Claritin line were $610 M. Domestic sales of Nasonex increased 2% to $63 M in 1Q 2001. Sales of the Vanceril (beclomethasone dipropionate) line of orally inhaled steroids for asthma and of Vancenase (beclomethasone dipropionate) Nasal Spray were down sharply due to manufacturing issues. In anti-infective/anticancer, US combined sales of Intron A, **Peg**

-**Intron** and Rebetron Combination Therapy totalled $187 M. Sales of dermatologicals, including Lotrisone (clotrimazole and betamethasone dipropionate) were down due to changes in the timing of trade buying. Reflecting increased utilization, 1Q 2001 domestic sales of **Temodar** rose to $26 M and, in cardiovasculars, sales of Integrilin increased 30% to $34 M. International pharmaceutical sales in 1Q 2001 increased 4% to $783 M. International sales were led by, in allergy/respiratory, Nasonex, with sales of $29 M; and, in antiinfective/anticancer, **Temodar**, with sales of $17 M, and Remicade. International combined sales of Intron A (including combination therapy with Rebetol and **Peg-Intron**) totalled $139 M for 1Q 2001. Sales of animal health products were down 2% for 1Q 2001. Schering-Plough is a research-based company engaged in the discovery, development, manufacturing and marketing of pharmaceutical products worldwide. Two included tables depict results of Schering-Plough Corp for 1Q ended Mar 2000 and 2001.

L248 ANSWER 35 OF 70 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2000:978409 PROMT
TITLE: Schering-Plough Annual Meeting Highlights Worldwide Performance, Commitment to Pharmaceutical Research.
SOURCE: PR Newswire, (25 Apr 2000) pp. 5365.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 978
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB KENILWORTH, N.J., April 25 /PRNewswire/ --
THIS IS THE FULL TEXT: COPYRIGHT 2000 PR Newswire Association, Inc.

L248 ANSWER 36 OF 70 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2000:636596 PROMT
TITLE: Schering-Plough Reports Sales, Earnings for 2000 Second Quarter, First Half.
SOURCE: PR Newswire, (25 Jul 2000) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 1376
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB 2000 Second Quarter Diluted Earnings Per Share Up 16% to 43 Cents
THIS IS THE FULL TEXT: COPYRIGHT 2000 PR Newswire Association, Inc.

L248 ANSWER 37 OF 70 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2000:917937 PROMT
TITLE: Schering-Plough Reports Sales, Earnings for 2000 Third Quarter, First Nine Months.
SOURCE: PR Newswire, (24 Oct 2000) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 1462
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB 2000 Third Quarter Diluted Earnings Per Share up 14% to 40 Cents
THIS IS THE FULL TEXT: COPYRIGHT 2000 PR Newswire Association, Inc.

L248 ANSWER 38 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:723116 CAPLUS
DOCUMENT NUMBER: 133:265657
TITLE: Melanoma therapy
INVENTOR(S): Rybak, Mary Ellen; Rose, Esther Helen
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1043026	A2	20001011	EP 2000-107101	20000406
EP 1043026	A3	20001220		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2000061175	A2	20001019	WO 2000-US9129	20000406
WO 2000061175	A3	20010201		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2000319195	A2	20001121	JP 2000-105524	20000406
JP 2001288109	A2	20011016	JP 2000-105526	20000406

PRIORITY APPLN. INFO.: US 1999-288366 A 19990408
JP 2000-105524 A3 20000406

AB Methods for treating treatment-naive as well as treatment-experienced patients having melanoma to increase the progression-free survival time involving administering a therapeutically effective amt. of **pegylated interferon**-alfa, e.g. preferably **pegylated interferon** alfa-2b, as adjuvant therapy to definitive surgery are disclosed.

L248 ANSWER 39 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:723115 CAPLUS
DOCUMENT NUMBER: 133:265656
TITLE: Renal cell **carcinoma** treatment
INVENTOR(S): Rose, Esther Helen; Rybak, Mary Ellen
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1043025	A2	20001011	EP 2000-107100	20000406
EP 1043025	A3	20001220		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2000061174	A2	20001019	WO 2000-US9127	20000406
WO 2000061174	A3	20010125		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

JP 2000319196	A2	20001121	JP 2000-105528	20000406
JP 2001288110	A2	20011016	JP 2000-105531	20000406

PRIORITY APPLN. INFO.: US 1999-288359 A 19990408
JP 2000-105528 A3 20000406

AB Methods for treating treatment-naive as well as treatment-experienced patients having RCC to achieve at least a partial **tumor** response involving administering a therapeutically effective amt. of **pegylated interferon**-alfa, e.g., **pegylated interferon** alfa-2b as monotherapy or in assocn. with a therapeutically effective amt. of IL-2 are disclosed.

L248 ANSWER 40 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:723114 CAPLUS
DOCUMENT NUMBER: 133:261520
TITLE: Chronic myeloid leukemia (CML) therapy
INVENTOR(S): Rybak, Mary Ellen; Rose, Esther Helen
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1043024	A2	20001011	EP 2000-107099	20000406
EP 1043024	A3	20001220		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

WO 2000061173	A2	20001019	WO 2000-US9038	20000405
WO 2000061173	A3	20010125		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

JP 2000309541	A2	20001107	JP 2000-104045	20000405

PRIORITY APPLN. INFO.: US 1999-288369 A 19990408
AB Methods for treating treatment-naive as well as treatment-experienced patients having CML to achieve at least a partial cytogenetic response involving administering a therapeutically effective amt. of **pegylated interferon**-.alpha., e.g., **pegylated interferon**-.alpha.-2b as monotherapy or in assocn. with a therapeutically effective amt. of Ara-C are disclosed.

L248 ANSWER 41 OF 70 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 2000:30313839 BIOTECHNO
TITLE: **Pegylated** alpha **interferon** is an

effective treatment for virulent venezuelan equine encephalitis virus and has profound effects on the host immune response to infection

AUTHOR: Lukaszewski R.A.; Brooks T.J.G.
CORPORATE SOURCE: R.A. Lukaszewski, CBD, Porton Down, Salisbury, Wiltshire SP4 0JQ, United Kingdom.
E-mail: rlukaszewski@hotmail.com

SOURCE: Journal of Virology, (2000), 74/11 (5006-5015), 42 reference(s)
CODEN: JOVIAM ISSN: 0022-538X
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Venezuelan equine encephalitis virus (VEEV) is a highly infectious alphavirus endemic in parts of Central and South America. The disease is transmitted by mosquitoes, and the natural reservoir is the small rodent population, with epidemics occurring in horses and occasionally humans. Following infection, VEEV replicates in lymphoid tissues prior to invasion of the central nervous system. Treatment of VEEV-infected BALB/c mice with **polyethylene glycol**-conjugated alpha **interferon** (**PEG** IFN-.alpha.) results in a greatly enhanced survival from either a subcutaneous or an aerosol infection. Virus is undetectable within **PEG** IFN-.alpha.-treated individuals by day 30 postinfection (p.i.). Treatment results in a number of changes to the immune response characteristics normally associated with VEEV infection. Increased macrophage activation occurs in **PEG** IFN-.alpha.-treated BALB/c mice infected with VEEV. The rapid activation of splenic CD4, CD8, and B cells by day 2 p.i. normally associated with VEEV infection is absent in **PEG** IFN-.alpha.-treated mice. The high **tumor** necrosis factor alpha production by macrophages from untreated mice is greatly diminished in **PEG** IFN-.alpha.-treated mice. These results suggest key immunological mechanisms targeted by this lethal alphavirus that can be modulated by prolonged exposure to IFN-.alpha..

L248 ANSWER 42 OF 70 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 2000:30471275 BIOTECHNO
TITLE: Controlled-release, **pegylation**, liposomal formulations: New mechanisms in the delivery of injectable drugs

AUTHOR: Reddy K.R.
CORPORATE SOURCE: Dr. K.R. Reddy, Division of Hepatology, Center for Liver Diseases, Univ. of Miami School of Medicine, 1500 NW 12th Ave., Miami, FL 33136, United States.
E-mail: RReddy@med.miami.edu

SOURCE: Annals of Pharmacotherapy, (2000), 34/7-8 (915-923), 63 reference(s)
CODEN: APHRER ISSN: 1060-0280
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English; Spanish; French

AB OBJECTIVE: To review recent developments in novel injectable drug delivery mechanisms and outline the advantages and disadvantages of each. DATA SOURCES: A MEDLINE (1995-January 2000) search using the terms **polyethylene glycol**, liposomes, polymers, polylactic acid, and controlled release was conducted. Additional references were identified by scanning bibliographies. STUDY SELECTION AND DATA EXTRACTION: All articles were considered for inclusion. Abstracts were

included only if they were judged to add critical information not otherwise available in the medical literature. DATA SYNTHESIS: A number of systems that alter the delivery of injectable drugs have been developed in attempts to improve pharmacodynamic and pharmacokinetic properties of therapeutic agents. New drug delivery systems can be produced either through a change in formulation (e.g., continuous-release products, liposomes) or an addition to the drug molecule (e.g., **pegylation**). Potential advantages of new delivery mechanisms include an increased or prolonged duration of pharmacologic activity, a decrease in adverse effects, and increased patient compliance and quality of life. Injectable continuous-release systems deliver drugs in a controlled, predetermined fashion and are particularly appropriate when it is important to avoid large fluctuations in plasma drug concentrations. Encapsulating a drug within a liposome can produce a prolonged half-life and a shift of distribution toward tissues with increased capillary permeability (e.g., **tumors**, infected tissue). **Pegylation** provides a method for modification of therapeutic proteins to minimize many of the limitations (e.g., poor stability, short half-life, immunogenicity) associated with these agents. CONCLUSIONS: **Pegylation** of therapeutic proteins is an established process with new applications. However, not all **pegylated** proteins are alike, and each requires optimization on a protein-by-protein basis to derive maximum clinical benefit. The language required to describe each **pegylated** therapeutic protein must be more precise to accurately distinguish each protein's differential pharmacologic properties.

L248 ANSWER 43 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:320146 BIOSIS
DOCUMENT NUMBER: PREV200100320146
TITLE: **PEG-interferon** alpha-2A (PegasysTM) with or without cytarabine in patients with relapsed or refractory chronic phase CML.
AUTHOR(S): Talpaz, M. (1); Cortes, J. (1); O'Brien, S. (1); Wenske, C. (1); Rittweger, K.; Rakhit, A.; Hooftman, L.; Kantarjian, H. (1)
CORPORATE SOURCE: (1) Bioimmunotherapy and Leukemia, UT MD Anderson Cancer Center, Houston, TX USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 736a-737a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Attachment of a 40 kDa branched **polyethylene glycol** (**PEG**) molecule to **interferon** alpha-2A (IFN) results in a novel IFN with sustained absorption and prolonged half-life that can be administered once weekly. Of 43 patients with heavily pre-treated chronic-phase CML (25 males, 18 females; aged 24 to 69 years) in this dose finding study, 27 were treated with PegasysTM monotherapy (5 cohorts: 270, 360, 450, 540, 630mug qw) and 16 received combination PegasysTM (3 cohorts; 450 or 540mug qw + ara-C 10mg/day or 20 mg/M2 X 20 d/month). All patients had previous CML therapy: IFN (43), ara-C (29), hydroxyurea (27). Median disease duration was 4.5 years. DLT occurred within the first 28 days of therapy with the two PegasysTM 540mug + ara-C combinations (one patient each with grade 4 neutropenia or grade 3 skin rash/mucositis, and 2 patients with grade 3 thrombocytopenia), but not in any monotherapy

cohorts. Hence, MTD-1 for the combination only was PegasysTM 450mug qw + ara-C 10mg/day. Other commonly reported adverse events were: headache, fatigue, nausea, vomiting, diarrhea, myalgia, fever, chills, night sweats, decreased appetite, arthralgia, insomnia, dizziness and injection site pain. Mild ALT elevations occurred in some patients at all dose levels, and grade 2/3 ALT resulted in dose reduction in 5 patients. Two patients on monotherapy reached grade 2 ALT at week 13, and 3 patients on combination between weeks 3 and 9. Toxicity was managed by withholding drug (average 6 weeks) until ALT normalized, then restarting drug at a lower dose. When dose modification was instituted earlier, ALT was maintained at a lower level. Of 37 patients evaluable for efficacy, 32 (84%) had a complete hematologic response (7/14 on ara-C), and 7 (19%) achieved a major cytogenetic response (3/13 on ara-C). With a median follow-up of 12 months, overall survival is 95%. Of 25 patients who began treatment over a year ago, 14 completed the 52 week study, and 8 continue treatment. Another 14 patients are still on study (7 to 11 months). Once weekly sc dosing with PegasysTM in CML patients maintains drug levels at close to peak between 48 and 168 hours post dose. MTD was not reached in PegasysTM monotherapy cohorts, whereas with the addition of ara-C, it was reached at 540mug. A multi-center, randomized Phase III trial of PegasysTM vs IFN is underway in newly diagnosed CML.

L248 ANSWER 44 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:320145 BIOSIS
DOCUMENT NUMBER: PREV200100320145
TITLE: Updated phase I study of **polyethylene glycol** formulation of **interferon** alpha-2B (**PEG Intron**; Schering 54031) in Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+CML.
AUTHOR(S): Talpaz, Moshe (1); O'Brien, Susan (1); Rose, Esther; Shan, Jianqin (1); Kantarjian, Hagop M. (1)
CORPORATE SOURCE: (1) Bioimmunotherapy, Leukemia, MD Anderson Cancer Center, Houston, TX USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 736a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Patient compliance to prolonged interferon-alpha (IFN-alpha) therapy is important for obtaining therapeutic benefit in CML. IFN-alpha therapy is cumbersome, given as a daily subcutaneous injection, and is associated with dose-limiting toxicities in 10% to 50% of patients. Polyethylene glycol (PEG) attached to IFN-alpha prolongs its half-life, and may be associated with reduced toxicity and improved efficacy. In a phase I study, we evaluated the maximally tolerated dose (MTD) and dose-limiting toxicities (DLT) of **PEG Intron**, and response profiles among patients who failed IFN-alpha therapy. **PEG Intron** was given as a weekly subcutaneous injection with a starting dose of 0.75mug/kg weekly and dose escalations to 1.5,3,4.5,6,7.5, and 9mug/kg. 27 patients were treated; median age was 47 years. All had failed IFN-alpha therapy because of hematologic resistance (9 patients), cytogenetic resistance (12 patients), or IFN-alpha intolerance (6 patients). 18 patients had active disease and 9 were in complete hematologic response (CHR), 6 of them with Ph-suppression. The MTD was defined at 7.5 to 9mug/kg weekly. The DLT included severe fatigue, neurotoxicity, liver

function abnormalities, and myelosuppression. These occurred with longer administration of **PEG Intron**. The proposed dose of **PEG Intron** for phase II studies was 6mug/kg weekly. Among 18 patients treated with active disease, 6 achieved CHR (33%) and 3 had a partial hematologic response (PHR), for an overall response rate of 50%. Only one patient (6%) had a cytogenetic response (complete). Among 9 patients treated in CHR, 8 (90%) improved their cytogenetic response to complete (5 patients), or partial (3 patients) cytogenetic response. All 6 patients intolerant to IFN-alpha tolerated **PEG Intron**, and 4 of them improved their cytogenetic response. Overall, 13 of 27 patients (48%) who had "failed" IFN-alpha therapy had a favorable response to **PEG-Intron** (CHR or improved cytogenetic response). The proposed **PEG Intron** dose of 6mug/kg/week is equivalent to IFN-alpha of 15MU/m2daily, i.e. at least 3 times the dose of IFN-alpha given in previous CML studies. In summary, **PEG intron** appeared to be easier to deliver (once weekly), better tolerated, and perhaps more effective than IFN-alpha.

L248 ANSWER 45 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:684305 CAPLUS
DOCUMENT NUMBER: 134:141466
TITLE: A phase II study of temozolomide vs. procarbazine in patients with glioblastoma multiforme at first relapse
AUTHOR(S): Yung, W. K. A.; Albright, R. E.; Olson, J.; Fredericks, R.; Fink, K.; Prados, M. D.; Brada, M.; Spence, A.; Hohl, R. J.; Shapiro, W.; Glantz, M.; Greenberg, H.; Selker, R. G.; Vick, N. A.; Rampling, R.; Friedman, H.; Phillips, P.; Bruner, J.; Yue, N.; Osoba, D.; **Zaknoen, S.**; Levin, V. A.
CORPORATE SOURCE: UTMD Anderson Cancer Center, Department of Neuro-Oncology, Houston, TX, 77030, USA
SOURCE: Br. J. Cancer (2000), 83(5), 588-593
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Harcourt Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A randomized, multicenter, open-label, phase II study compared temozolomide (TMZ), an oral second-generation alkylating agent, and procarbazine (PCB) in 225 patients with glioblastoma multiforme at first relapse. Primary objectives were to det. progression-free survival (PFS) at 6 mo and safety for TMZ and PCB in adult patients who failed conventional treatment. Secondary objectives were to assess overall survival and health-related quality of life (HRQL). TMZ was given orally at 200 mg/m2/day or 150 mg/m2/day (prior chemotherapy) for 5 days, repeated every 28 days. PCB was given orally at 150 mg/m2/day or 125 mg/m2/day (prior chemotherapy) for 28 days, repeated every 56 days. HRQL was assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30 [+3]) and the Brain Cancer Module 20 (BCM20). The 6-mo PFS rate for patients who received TMZ was 21%, which met the protocol objective. The 6-mo PFS rate for those who received PCB was 8% (P = 0.008, for the comparison). Overall PFS significantly improved with TMZ, with a median PFS of 12.4 wk in the TMZ group and 8.32 wk in the PCB group (P = 0.0063). The 6-mo overall survival rate for TMZ patients was 60% vs. 44% for PCB patients (P = 0.019). Freedom from disease progression was assocd. with maintenance of HRQL, regardless of treatment received. TMZ had an acceptable safety profile; most adverse events were mild or moderate in severity.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L248 ANSWER 46 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:508661 BIOSIS
DOCUMENT NUMBER: PREV200000508661
TITLE: New treatment approaches for chronic myelogenous leukemia.
AUTHOR(S): Faderl, Stefan; Kantarjian, Hagop M.; Talpaz, Moshe; O'Brien, Susan (1)
CORPORATE SOURCE: (1) Department of Leukemia, University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX, 77030 USA
SOURCE: Seminars in Oncology, (October, 2000) Vol. 27, No. 5, pp. 578-586. print.
ISSN: 0093-7754.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English

L248 ANSWER 47 OF 70 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-13415 DRUGU P T S
TITLE: Phase I study of **pegylated-interferon** alpha-2a (PEGASYS) in renal cell **carcinoma**.
AUTHOR: Berg W J; Rakhit A; Ginsberg M; Rittweger K; Hooftman L; Fettner S; Yu R; Motzer R J
CORPORATE SOURCE: Memorial-Sloan-Kettering-Cancer-Cent.; Roche
LOCATION: New York, N.Y.; Nutley, N.J., USA
SOURCE: ; Proc.Am.Soc.Clin.Oncol. (19, 36 Meet.; 341a, 2000) CODEN: ; 7790
AVAIL. OF DOC.: Memorial Sloan-Kettering Cancer Center, New York, NY, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB A Phase I study of s.c. pegylated IFN-alpha-2a (PEG-IFN) in 27 previously untreated patients with advanced renal cell **carcinoma** is reported. Side-effects were mainly mild to moderate and were similar to those of standard IFN (flu-like symptoms). Systemic drug exposure was dose-dependent. PEG-IFN was active with tolerable side-effects and demonstrated pharmacokinetic advantages in patients with renal cell **carcinoma**. (conference abstract: 36th Annual Meeting of the American Society of Clinical **Oncology**, New Orleans, Louisiana, USA, 2000).

L248 ANSWER 48 OF 70 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 2000:30165168 BIOTECHNO
TITLE: Cytokines delivered by biodegradable microspheres promote effective suppression of human **tumors** by human peripheral blood lymphocytes in the SCID-Winn model
AUTHOR: Egilmez N.K.; Jong Y.S.; Hess S.D.; Jacob J.S.; Mathiowitz E.; Bankert R.B.
CORPORATE SOURCE: Dr. N.K. Egilmez, Roswell Park Cancer Institute, Department of Immunology, Elm and Carlton Streets, Buffalo, NY 14263, United States.
SOURCE: Journal of Immunotherapy, (2000), 23/2 (190-195), 13 reference(s)
CODEN: JOIME7 ISSN: 1053-8550
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A new technology for the local and sustained delivery of

immunostimulatory molecules to the **tumor** environment for **cancer** immunotherapy was evaluated. The ability of cytokines delivered by biodegradable microspheres to promote the **antitumor** activity of human peripheral blood lymphocytes (PBL) was tested in a human PBL, human **tumor**, and SCID mouse (SCID-Winn) model. Co-engraftment of human recombinant IL-12-loaded microspheres with human PBL and **tumors** in SCID mice promoted complete **tumor** suppression in as many as 100% of the mice, whereas microspheres loaded with **polyethyleneglycol**-interleukin-2 suppressed but did not eliminate the growth of **tumor** xenografts. Control microspheres (loaded with bovine serum albumin) in the presence of human PBL or cytokine-loaded microspheres in the absence of human PBL had no **tumor**-suppressive effect. Coincident with the enhancement of the human PBL-mediated **antitumor** activity in mice treated with IL-12- loaded microspheres was the production and release of human IFN-.gamma. indicating that IL-12 released from the microspheres results in the activation of the engrafted human PBL. The results establish that biodegradable microspheres represent an effective tool for the local and sustained delivery of cytokines to the **tumor** environment for **cancer** immunotherapy.

L248 ANSWER 49 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000277255 EMBASE
TITLE: [First clinical results with **PEG-interferon** alfa-2b in chronic myeloid leukemia (CML)].
ERSTE KLINISCHE ERGEBNISSE MIT PEG-IFN-ALFA-2B BEI CML.
AUTHOR: Roos M.
SOURCE: Onkologie Service Aktuell, (2000) -/3 (7).
ISSN: 0949-3441 CODEN: OSAKFB
COUNTRY: Germany
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 025 Hematology
037 Drug Literature Index
LANGUAGE: German

L248 ANSWER 50 OF 70 CBNB COPYRIGHT 2002 EI
ACCESSION NUMBER: 16(43):60759 CBNB
TITLE: Schering-Plough reports sales, earnings for 3Q 2000, first nine months of 2000. [4 tables]
SOURCE: Schering-Plough 3Q and nine months of 2000 results (24 Oct 2000)
Availability: Schering-Plough Corp, One Giralda Farms, Madison, NJ 07940-1010, USA, Tel: +1 973 822 7000, Fax: +1 973 822 7048, Website: http://www.schering-plough.com
DOCUMENT TYPE: Journal; Company Publication
LANGUAGE: English
AB Schering-Plough Corp reported financial results for 3Q and nine months ended Sep 2000. Net income for 3Q 2000 was $591 M (net income of $518 M in 3Q 1999). For 3Q 2000, sales were $2.4 bn (+7% over $2.2 bn in 3Q 1999). Net income was $1.9 bn for nine months of 2000 (net income of $1.6 bn in nine months of 1999). Sales for first nine months of 2000 totalled $7.4 bn (8% over $6.9 bn in nine months of 1999). Worldwide pharmaceutical sales increased 8% to $2.1 bn during 3Q 2000. Worldwide sales of Claritin (loratadine) line of nonsedating antihistamines rose 10% to $787 M for 3Q 2000. The combined worldwide sales of the antiviral/anticancer agent Intron A (**interferon** alfa-2b); **Peg-Intron** (**PEG-interferon** alfa-2b), a longer-acting form of Intron A; and Rebetron Combination

Therapy containing Intron A and Rebetol (ribavirin, USP) Capsules, totalled $338 M for 3Q 2000. Sales of the company's nasal inhaled steroid franchise increased 29% to $126 M during 3Q 2000, led by Nasonex (mometasone furoate monohydrate) Nasal Spray 50 mcg, a once-daily nasal spray for allergies, with a 44% increase in sales to $98 M. Also contributing to higher worldwide sales were Integrilin (eptifibatide) Injection, a platelet aggregation inhibitor for the treatment of acute coronary syndromes, with sales of $52 M, and **Temodar** (temozolomide), for treating certain types of brain tumours recorded $37 M sales. US pharmaceutical sales for 3Q 2000 increased 5% to $1.3 bn. Sales of the Claritin line increased 12% to $700 M for 3Q 2000. US combined sales of Intron A and Rebetron Combination Therapy increased 12% to $186 M. US sales of the nasal inhaled steroid franchise increased 22% to $104 M during 3Q 2000, led by Nasonex, with a 36% increase in sales to $78 M for 3Q 2000. Other products contributing to higher third quarter domestic sales were Integrilin, with sales of $48 M, and **Temodar**, with sales of $21 M. International pharmaceutical sales for 3Q 2000 increased 13% to $746 M. Sales growth was led by Intron A (including combination therapy with Rebetol) and **Peg-Intron**, which combined rose 41% to $153 M, and Nasonex, with sales of $20 M. Also contributing to higher international sales were **Temodar** and Remicade (infliximab), for the treatment of rheumatoid arthritis and Crohn's disease. Worldwide sales of animal health products for 3Q 2000 increased 9% to $176 M. Worldwide pharmaceutical sales for nine months of 2000 rose 9% to $6.3 bn. Sales of domestic pharmaceuticals increased 9% to $4 bn for nine months of 2000. Schering-Plough is a research- based company engaged in the discovery, development, manufacturing and marketing of pharmaceutical products worldwide. The unaudited report of financial results, and net sales by major therapeutic category of Schering-Plough for three months and nine months of 1999 and 2000 are included in four tables.

L248 ANSWER 51 OF 70 CANCERLIT
ACCESSION NUMBER: 1999701711 CANCERLIT
DOCUMENT NUMBER: 99701711
TITLE: Phase I Study of **Polyethylene Glycol** (**PEG**) **Interferon** Alpha-2B (**PEG INTRON**) in Patients with Solid **Tumors** (Meeting abstract).
AUTHOR: Bukowski Ronal; Ernstoff Mar; Gore Marti; Amato Rober; Rose Esthe; Rybak Mary Elle; Gupta Sami
CORPORATE SOURCE: Schering Plough Research Institute, Kenilworth, NJ.
SOURCE: Proc Annu Meet Am Soc Clin Oncol, (1999). Vol. 18, pp. A1719.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199910

AB Alpha interferon (<FONT>a-IFN) is commonly used in the management of solid **tumors** and hematologic malignancies. Treatment requires frequent injections and is associated with significant constitutional side effects. **PEG Intron** is formed by covalent attachment of a molecule of PEG to the <FONT>a-IFN molecule, resulting in a conjugate with a significantly longer half-life than <FONT>a-IFN, and requiring less frequent administration. The safety of **PEG Intron** was evaluated in 35 patients (pts) with advanced solid **tumors**. Cohorts of 3-6 pts received **PEG Intron** by weekly subcutaneous (SC) injections at dose levels of 0.75, 1.5, 3.0, 4.5, 6.0 or 7.5 <FONT>mg/kg for 12 weeks. In addition to standard safety evaluations, measurement of the kinetic (PK) profile of **PEG Intron**

was performed during Weeks 1 and 4. The age range was 37-77; 21 were male. The majority of pts had renal cell **carcinoma** (22) or melanoma (6). The most frequently reported adverse experiences were anorexia, nausea, fatigue, headache, chills, fever and redness at the injection site. Most were Grade 1-2 and are consistent with the known safety profile of <FONT>a-IFN. Reversible Grade 3 toxicities included renal insufficiency, nausea/vomiting/dehydration and neutropenia. With prolonged dosing, fatigue was the most prominent symptom, while most other reported side effects were lessened in intensity. PK analysis showed sustained serum levels of <FONT>a-IFN activity, and a dose-related increase in the area-under-the-curve (AUC). Objective partial responses (>50% **tumor** shrinkage) were demonstrated in melanoma (2 pts), adrenal **carcinoma** (1 pt) and renal cell **carcinoma** (3 pts). Based on overall tolerability, a dose of 6.0 <FONT>mg/kg/wk of **PEG Intron** is suggested for further evaluation. (C) American Society of Clinical **Oncology** 1999.

L248 ANSWER 52 OF 70 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2000:169630 PROMT
TITLE: Plowing along.
AUTHOR(S): Brown, Joseph
SOURCE: Med Ad News, (Sept 1999) Vol. 18, No. 9, pp. 248. ISSN: 1067-733X.
PUBLISHER: Engel Publishing Partners
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 5039
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB In 1998, Schering-Plough reaped the benefits of a solid sales performance from its blockbuster products, Claritin and Intron A
THIS IS THE FULL TEXT: COPYRIGHT 1999 Engel Publishing Partners

Subscription: $85.00 per year. Published monthly. 820 Bear Tavern Rd, West Trenton, NJ 08628. FAX 609-530-0207.

L248 ANSWER 53 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:708645 CAPLUS
DOCUMENT NUMBER: 131:327540
TITLE: Polyol-IFN-beta conjugates
INVENTOR(S): El Tayar, Nabil; Roberts, Michael J.; Harris, Milton; Sawlivich, Wayne
PATENT ASSIGNEE(S): Applied Research Systems Ars Holding N.V., Neth. Antilles
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955377	A2	19991104	WO 1999-US9161	19990428
WO 9955377	A3	19991229		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,

MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9937674	A1	19991116	AU 1999-37674	19990428
BR 9910023	A	20001226	BR 1999-10023	19990428
EP 1075281	A2	20010214	EP 1999-920094	19990428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2000005337	A	20001228	NO 2000-5337	20001023

PRIORITY APPLN. INFO.: US 1998-83339 P 19980428
WO 1999-US9161 W 19990428

AB PEG-IFN-.beta. conjugates, where a PEG moiety is covalently bound to Cys17 of human IFN-.beta., are produced by a process of site specific PEGylation with a thiol reactive PEGylating agent. A pharmaceutical compn. and a method for treating infections, **tumors** and autoimmune and inflammatory diseases are also provided. The invention further relates to a method for the stepwise attachment of PEG moieties in series to a polypeptide, and more particularly to IFN-.beta.. Human interferon-.beta. was coupled to PEG Me 2-pyridyldithio ether and the conjugate maintained a level of antiviral activity superior th that of freshly prepd. parenteral lot of IFN-.beta..

L248 ANSWER 54 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:527133 CAPLUS
DOCUMENT NUMBER: 133:109999
TITLE: Compound alpha-interferon lozenge and its preparing method
INVENTOR(S): Cao, Xuetao; Ju, Dianwen; Tao, Qun
PATENT ASSIGNEE(S): Huachen Biological Technology Inst., Shanghai, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1227125	A	19990901	CN 1998-105384	19980225

AB The alpha interferon lozenge is composed of 100-500 IU alpha-interferon, 1-10 kIU interleukin-2, and medicinal adjuvant, preferably 250 IU alpha-interferon, 2.5 kIU interleukin-2, and medicinal adjuvant. The medicinal adjuvant is selected from one or more of human serum albumin, bovine serum protein, polyethylene glycol, mannitol, lactose, glucose, starch, Mg stearate, and dextrin. The alpha interferon lozenge is prepd. by mixing medicinal adjuvant, sieving, drying to obtain blank granule; mixing medicinal adjuvant with alpha-interferon and interleukin-2, freezing to dry, mixing with the blank granule; and tableting. The lozenge is used for treatment of virus infection (such as hepatitis B and C) and or **tumor**.

L248 ANSWER 55 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:542710 CAPLUS
DOCUMENT NUMBER: 133:109998
TITLE: Beta-interferon lozenge and its preparing method
INVENTOR(S): Cao, Xuetao; Ju, Dianwen; Tao, Qun
PATENT ASSIGNEE(S): Huachen Biological Technology Inst., Shanghai, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 13 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1227124	A	19990901	CN 1998-105383	19980225

AB The beta interferon lozenge is composed of 1-10 kIU beta-interferon and medicinal adjuvant. The medicinal adjuvant is selected from one or more of human serum albumin, bovine serum protein, polyethylene glycol, mannitol, lactose, glucose, starch, Mg stearate, and dextrin. The beta-interferon lozenge may contain 100-1,000 IU alpha-interferon and/or 1-10 kIU interleukin-2. The beta interferon lozenge is prepd. by mixing medicinal adjuvant, sieving, drying to obtain blank granule; spraying beta-interferon soln. in the blank granule; drying, and tableting. The lozenge is used for treatment of virus infection and/or **tumor**.

L248 ANSWER 56 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:201495 CAPLUS
DOCUMENT NUMBER: 132:202786
TITLE: Multicenter phase II trial of temozolomide in patients with anaplastic astrocytoma or anaplastic oligoastrocytoma at first relapse. [Erratum to document cited in CA132:131891]
AUTHOR(S): Yung, W. K. Alfred; Prados, Michael D.; Yaya-Tur, Ricardo; Rosenfeld, Steven S.; Brada, Michael; Friedman, Henry S.; Albright, Robert; Olson, Jeffrey; Chang, Susan M.; O'Neill, Alison M.; Friedman, Allan H.; Bruner, Janet; Yue, Nancy; Dugan, Margaret; **Zaknoen, Sara**; Levin, Victor A.
CORPORATE SOURCE: University of Texas M.D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: J. Clin. Oncol. (1999), 17(11), 3693
CODEN: JCONDN; ISSN: 0732-183X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two corrections are given for the Appendix that lists the participants in the Temodal Brain Tumor Study Group. Dr. F. Lejeune's institution is the Center Pluridisciplinaire d'Oncologie, CHUV, Lausanne, Suisse. Dr. P-Y. Dietrich of the Division Oncologie-Hematologie, Hopital Cantonal, Geneva, Suisse, was omitted and should be included.

L248 ANSWER 57 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:631895 CAPLUS
DOCUMENT NUMBER: 132:131891
TITLE: Multicenter phase II trial of temozolomide in patients with anaplastic astrocytoma or anaplastic oligoastrocytoma at first relapse
AUTHOR(S): Yung, W. K. Alfred; Prados, Michael D.; Yaya-Tur, Ricardo; Rosenfeld, Steven S.; Brada, Michael; Friedman, Henry S.; Albright, Robert; Olson, Jeffrey; Chang, Susan M.; O'Neill, Alison M.; Friedman, Allan H.; Bruner, Janet; Yue, Nancy; Dugan, Margaret; **Zaknoen, Sara**; Levin, Victor A.
CORPORATE SOURCE: University of Texas M.D. Anderson Cancer Center, Houston, TX, 77030, USA

SOURCE: J. Clin. Oncol. (1999), 17(9), 2762-2771
CODEN: JCONDN; ISSN: 0732-183X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: To det. the antitumor efficacy and safety profile of temozolomide in patients with malignant astrocytoma at first relapse. Patients and Methods: This open-label, multicenter, phase II trial enrolled 162 patients (intent-to-treat [ITT] population). After central histol. review, 111 patients were confirmed to have had an anaplastic astrocytoma (AA) or anaplastic mixed oligoastrocytoma. Chemotherapy-naive patients were treated with temozolomide 200 mg/m2/d. Patients previously treated with chemotherapy received temozolomide 150 mg/m2/d; the dose could be increased to 200 mg/m2/d in the absence of grade 3/4 toxicity. Therapy was administered orally on the first 5 days of a 28-day cycle. Results: Progression-free survival (PFS) at 6 mo, the primary protocol end point, was 46% (95% confidence interval, 38% to 54%). The median PFS was 5.4 mo, and PFS at 12 mo was 24%. The median overall survival was 13.6 mo, and the 6- and 12-mo survival rates were 75% and 56%, resp. The objective response rate detd. by independent central review of gadolinium-enhanced magnetic resonance imaging scans of the ITT population was 35% (8% complete response [CR], 27% partial response [PR]), with an addnl. 26% of patients with stable disease (SD). The median PFS for patients with SD was 4.4 mo, with 33% progression-free at 6 mo. Maintenance of progression-free status and objectively assessed response (CR/PR/SD) were both assocd. with health-related quality-of-life (HQL) benefits. Adverse events were mild to moderate, with hematol. side effects occurring in less than 10% of patients. Conclusion: Temozolomide demonstrated good single-agent activity, an acceptable safety profile, and documented HQL benefits in patients with recurrent AA.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L248 ANSWER 58 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:44333 BIOSIS
DOCUMENT NUMBER: PREV200000044333
TITLE: Phase I study of **pegylated-interferon** alpha-2a (PEGASYSTM) in patients with chronic myelogenous leukemia (CML.
AUTHOR(S): Talpaz, M. (1); O'Brien, S.; Cortes, J.; Giles, F.; Rittweger, K.; Hooftman, L.; Rakhit, A.; Kantarjian, H.
CORPORATE SOURCE: (1) Department of Bioimmunotherapy, U.T.M.D. Anderson Cancer, Houston, TX USA
SOURCE: Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1, pp. 530a.
Meeting Info.: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December 3-7, 1999 The American Society of Hematology . ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L248 ANSWER 59 OF 70 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-44952 DRUGU T G S
TITLE: Phase I study of **polyethylene glycol** (**PEG**) **interferon** alpha-2B (**PEG INTRON**) in patients with solid **tumors**.
AUTHOR: Bukowski R; Ernstoff M; Gore M; Amato R; Rose E; Rybak M E; Gupta S
CORPORATE SOURCE: Schering-Plough

LOCATION: Kenilworth, N.J., USA
SOURCE: ; Proc.Am.Soc.Clin.Oncol. (18, 35 Meet., 446a, 1999)
CODEN: ; 7790
AVAIL. OF DOC.: Schering Plough Research Institute, Kenilworth, NJ, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The effects of s.c. **polyethylene glycol** (**PEG**) **interferon** alpha-2b (IFN-alpha2b, Intron) were examined in a phase I trial of 35 patients with solid **tumors**. There was some response in patients treated with **PEG-intron**. Adverse effects reported include anorexia, nausea, fatigue, headache, chills, fever, injection site redness, renal insufficiency, nausea, vomiting, dehydration and neutropenia. Further studies are suggested to examine a dose of 6.0 ug/kg/wk of **PEG-intron** as the data from this study showed that the doses used were well tolerated. (conference abstract: 35th Annual Meeting of the American Society of Clinical **Oncology**, Atlanta, Georgia, USA, 1999).

L248 ANSWER 60 OF 70 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 1999:29329724 BIOTECHNO
TITLE: The role of cytokines in rheumatoid arthritis: Inhibition of cytokines in therapeutic trials
AUTHOR: Moreland L.W.
CORPORATE SOURCE: Dr. L.W. Moreland, Clinic. Immunology/Rheumatology Div., University of Alabama, 068 Spain Rehabilitation Center, 1717 Sixth Avenue South, Birmingham, AL 35294-7201, United States.
SOURCE: Drugs of Today, (1999), 35/4-5 (309-319), 67 reference(s)
CODEN: MDACAP ISSN: 0025-7656
DOCUMENT TYPE: Journal; Conference Article
COUNTRY: Spain
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Although the precise role(s) of cytokines in rheumatoid arthritis (RA) is still being investigated, increasing evidence implicates interleukin (IL)- 1 and **tumor** necrosis factor (TNF)-.alpha. as contributing importantly to the inflammatory, and perhaps destructive manifestations of the disease. Several natural endogenous inhibitors of IL-1 and TNF-.alpha. have been identified; these include interleukin-1 receptor antagonist (IL-1RA), soluble IL-1 receptors (sIL-1R), and soluble TNF-.alpha. receptors (sTNFR). Although increased levels of these natural inhibitors occur in sera and at sites of inflammation in patients with RA, there is an excess of IL-1 and TNF-.alpha. in comparison with their respective natural inhibitors that favors the proinflammatory actions of these cytokines. Therefore, a potential therapeutic maneuver for treating RA is to neutralize these implicated cytokines. Biologic agents aimed at inhibiting the proinflammatory activities of these cytokines thus far have included cytokine receptor antagonists, anticytokine monoclonal antibodies (MAbs), fusion molecules consisting of soluble cytokine receptors combined with human fusion protein (Fc) constructs or **polyethylene glycol** (**PEG**), and counter-regulatory cytokines which oppose actions of the target cytokine (e.g., IL-10, IL-4 and IL-11). Inhibitors of the processing and synthesis of IL-1 and TNF-.alpha. are also under development. The encouraging clinical results observed in short-term trials of TNF-.alpha. and IL-1 inhibitors using sTNFR:Fc fusion proteins, anti-TNF MAbs and recombinant human IL-1 receptor antagonist (rhuIL-1 RA) clearly warrant further

studies not only to determine whether these agents are capable of modifying the destructive component of the disease, but also whether they can be administered safely for long periods. Pivotal trials with these agents have potential therapeutic applicability to other autoimmune and inflammatory disorders.

L248 ANSWER 61 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:738215 CAPLUS
DOCUMENT NUMBER: 130:133766
TITLE: Interferon induction: a mechanism to explain **antitumor** activity and defective AKT retrovirus production by Lentinus edodes extract
AUTHOR(S): Kumar, C. Sudhir; Ng, M. L.
CORPORATE SOURCE: Department of Microbiology, Lower Kent Ridge Crescent, Faculty of Medicine, National University of Singapore, Singapore, 119260, Singapore
SOURCE: Electron Microsc. 1998, Proc. Int. Congr., 14th (1998) , Volume 4, 677-678. Editor(s): Calderon Benavides, Hector A.; Jose Yacaman, Miguel. Institute of Physics Publishing: Bristol, UK.
CODEN: 66YYA4
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The shiitake mushroom (L. edodes) virus-like particles have been characterized to be a double-stranded RNA (ds-RNA). Since ds-RNA is potent inducer of **interferon**, the **PEG** ext. was evaluated for interferon induction. The ext. was found to induce interferon .gamma. prodn. after 7 days of oral administration to male AKR mice. Significant induction of interferon .gamma. was obsd. in six mice with most of them showing a peak 4 h after the last oral administration. Interferons are known to cause prodn. of defective virus. **Interferons** induced by the **PEG**-ext. accounts for the prodn. of defective retrovirus and **tumor** cells of apoptotic morphol. obsd. in earlier expts. The prodn. of non-infectious retroviral progenies may also be one of the mechanisms for its **antitumor** activity.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L248 ANSWER 62 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:102019 BIOSIS
DOCUMENT NUMBER: PREV199900102019
TITLE: Phase I study of **polyethylene glycol** (**PEG**) **interferon** alpha-2B (Intron-A) in CML patients.
AUTHOR(S): Talpaz, M. (1); Cortes, J.; O'Brien, S.; Keating, M.; Giles, F.; Rose, E.; Rybak, M. E.; Kantarjian, H.
CORPORATE SOURCE: (1) Dep. Bioimmunother., U.T.M.D. Anderson Cancer, Houston, TX USA
SOURCE: Blood, (Nov. 15, 1998) Vol. 92, No. 10 SUPPL. 1 PART 1-2, pp. 251A.
Meeting Info.: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998 The American Society of Heamatology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L248 ANSWER 63 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:783625 CAPLUS

DOCUMENT NUMBER: 128:47304
TITLE: **Polyethylene glycol** conjugates of .alpha.-**interferons**
INVENTOR(S): Bailon, Pascal Sebastian; Palleroni, Alicia Vallejo
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 809996	A2	19971203	EP 1997-108261	19970522
EP 809996	A3	19990414		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2203480	AA	19971130	CA 1997-2203480	19970423
ZA 9704583	A	19981117	ZA 1997-4583	19970526
CN 1167777	A	19971217	CN 1997-113049	19970529
JP 10067800	A2	19980310	JP 1997-139807	19970529
JP 2980569	B2	19991122		
NO 9702480	A	19971201	NO 1997-2480	19970530
AU 9723723	A1	19971204	AU 1997-23723	19970530
AU 725195	B2	20001005		
BR 9703421	A	19980915	BR 1997-3421	19970602

PRIORITY APPLN. INFO.: US 1996-18834 P 19960531

AB The authors disclose a new class of derivs. of interferon-.alpha. (IFN-.alpha.) produced by attachment of a branched moiety incorporating two linear polyethylene glycol chains. The attachment moiety is derived from mono-methoxy PEG derivatization of lysine at the .alpha. and .epsilon. amino groups followed by N-hydroxysuccinimide conjugation of IFN-.alpha.. Compared to unmodified IFN-.alpha., these derivs. have an increased half-life in circulation, reduced immunogenicity, decreased clearance, and increased anti-proliferative activity.

L248 ANSWER 64 OF 70 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1997-26217 DRUGU P M A
TITLE: Positional isomers of monopegylated interferon alpha-2a: isolation, characterization, and biological activity.
AUTHOR: Monkarsh S P; Ma Y; Aglione A; Bailon P; Ciolek D; DeBarbieri B; Graves M C; Hollfelder K; Michel H; Palleroni A; Porter J E; Russoman E; Roy S; Pan Y C E
CORPORATE SOURCE: Roche
LOCATION: Nutley, N.J., USA; Welwyn Garden City, U.K.
SOURCE: Anal.Biochem. (247, No. 2, 434-40, 1997) 4 Fig. 2 Tab. 16 Ref.
CODEN: ANBCA2 ISSN: 0003-2697
AVAIL. OF DOC.: Department of Analytical Research and Development, Hoffmann-La Roche Inc., Nutley, NJ 07110, U.S.A. (Y.C.E.P.).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB A newly developed ampholyte-free chromatofocusing-like cation-exchange HPLC method was used to separate the positional isomers of monopegylated (**PEG**-5000) **interferon**-alpha-2a (IFN), based on their local charge differences. The monopegylated protein was separated into 11 species on a sulfopropyl resin. Peptide mapping, sequencing and MS

analysis indicated that these species are positional isomers where each isomer represents a single polymer molecule conjugated to 1 specific Lys residue. Aliquots of the 11 PEG-IFN samples were analyzed for antiviral and antiproliferative activities. Samples 1-11 and PEG-IFN showed activity in the MDBK cell antiviral assay, between 1.2 and 7.2 x 10power7 IU/mg, indicating no significant difference between positional isomers. Antiproliferative activity was also seen vs human Daudi cells, again with no significant variation in IC50 (5.4-18.6 pM).

L248 ANSWER 65 OF 70 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 1995:25056298 BIOTECHNO
TITLE: Administration of systemic or local interleukin-2 enhances the anti-**tumor** effects of interleukin-12 gene therapy
AUTHOR: Pappo I.; Tahara H.; Robbins P.D.; Gately M.K.; Wolf S.F.; Barnea A.; Lotze M.T.
CORPORATE SOURCE: Department of Surgery, University of Pittsburgh,Pittsburgh, PA 15261, United States.
SOURCE: Journal of Surgical Research, (1995), 58/2 (218-226)
CODEN: JSGRA2 ISSN: 0022-4804
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Interleukin-12 (IL-12) is a cytokine with a wide variety of immunoregulatory activities. These include stimulation of **interferon**-.gamma. production, cytolytic activity of natural killer (NK) cells and T-cell subsets, the development of cellular immunity, and induction of maturation of Th1 cells. IL-12 also has potent anti-**tumor** activity in vivo. In the present study the possibility of enhanced anti-**tumor** activity was examined using a combination of local IL-12 by cytokine gene therapy at the **tumor** site, combined with systemic or local IL-2 delivery. NIH 3T3 fibroblasts transfected with the genes for both subunits of IL-12, p35 and p40, were used as the source of IL-12 therapy producing 240 HLRU/10.sup.6 cells/48 hr. In the first part of the study the effect of different regimens of systemic IL-2 delivery with local IL-12 administration on the size and growth rate of subcutaneous MCA-105 murine sarcoma was examined. Local IL-12 alone reduced the sizes of **tumors** after 32 days from 163 to 26.8 mm.sup.2 ($P < 0.002$). Adding the longer-acting **polyethylene-glycol**-modified IL-2 (**PEG** IL-2; 30,000 IU) for 5 days prevented the development of **tumors** in all treated mice compared to 1/3 mice treated with **PEG** IL-2 alone and 3/8 mice with IL-12, but this was a highly toxic therapy and most of the animals died. Administration of 60,000 IU of IL-2 on Days 1-5 postinoculation of **tumor**, delivered with IL-12 gene therapy, reduced the **tumor** growth rate compared to animals treated with IL-2 alone ($P < 0.02$) or IL-12 (0.1). After 30 days the mean **tumor** size was 1.2 mm.sup.2 compared to 17.8 mm.sup.2 with IL-12 alone, 85.4 mm.sup.2 with low-dose IL-2 ($P < 0.05$), and 46.2 mm.sup.2 in controls ($P < 0.03$). When IL-2 was added later, on Days 6-10, the additive effect of low-dose IL-2 with local IL-12 was less significant. Mean **tumor** sizes were 38.4 and 55 mm.sup.2. High-dose IL-2 abrogated the additive effect of IL-12. **Tumor** size was 111.4 compared to 55 mm.sup.2 with IL-12 alone. In the second part of the study the effect of local IL-2 produced by a transfected MC-38 murine colon adenocarcinoma cell line, producing IL-2 coupled with IL-12 gene therapy, was examined. **Tumor** cells and IL-12-producing NIH3T3 fibroblasts were injected at a ratio of 1:3 or 1:6. After 40 and 32 days, respectively, **tumor** sizes with the

combined treatment were 8.25 and 19.6 mm.sup.2 compared to 62.5 and 134.4 mm.sup.2 with IL-12 alone or 59.8 and 133 mm.sup.2 with IL-2 alone. In conclusion, local IL-12 produced at the **tumor** site during cytokine gene therapy when delivered with systemic or local low-dose IL-2 causes delayed **tumor** growth, when they are administered at the appropriate amounts and at the right time. The initial role of sequence, timing, and means of delivery may mimic the requirement for induction of an effective natural immune response.

L248 ANSWER 66 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 10
ACCESSION NUMBER: 1994:290148 BIOSIS
DOCUMENT NUMBER: PREV199497303148
TITLE: Pharmacodynamic and preliminary pharmacokinetic evaluation of **pegylated** derivatives of **interferon** -alpha-2a.
AUTHOR(S): Truitt, G. A. (1); Tarby, C. M. (1); Stern, L. L. (1); Tamborini, B. (1); Bontempo, J. B. (1); Nalin, C. (1); Dwyer, C.; Familletti, P.; Rosen, P.; Palmer, D.
CORPORATE SOURCE: (1) Dep. Oncol., Roche Res. Cent., Hoffmann-La Roche Inc., Nutley, NJ 07110 USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (1994) Vol. 35, No. 0, pp. 398. Meeting Info.: 85th Annual Meeting of the American Association for Cancer Research San Francisco, California, USA April 10-13, 1994 ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L248 ANSWER 67 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 11
ACCESSION NUMBER: 1994:289622 BIOSIS
DOCUMENT NUMBER: PREV199497302622
TITLE: The in vivo fate of **PEG-interferon** alpha-2a(Ro 25-3036) in **tumor** bearing mice.
AUTHOR(S): Palleroni, A. V.; Aglione, A.; Dvorozniak, M. T.; Truitt, G. A.
CORPORATE SOURCE: Hoffmann-La Roche Inc., Nutley, NJ 07110 USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (1994) Vol. 35, No. 0, pp. 310. Meeting Info.: 85th Annual Meeting of the American Association for Cancer Research San Francisco, California, USA April 10-13, 1994 ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L248 ANSWER 68 OF 70 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:6892 CAPLUS
DOCUMENT NUMBER: 120:6892
TITLE: Novel recombinant human IFN-.beta., its preparation, and pharmaceutical compositions containing it
INVENTOR(S): Siklosi, Thomas; Joester, Karl-eduard; Hofer, Hans
PATENT ASSIGNEE(S): BIOFERON Biochemische Substanzen GmbH und Co, Germany
SOURCE: Eur. Pat. Appl., 19 pp. CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 529300	A1	19930303	EP 1992-112427	19920721
EP 529300	B1	19981014		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
DE 4128319	A1	19930304	DE 1991-4128319	19910827
AT 172206	E	19981015	AT 1992-112427	19920721
ES 2121804	T3	19981216	ES 1992-112427	19920721

PRIORITY APPLN. INFO.: DE 1991-4128319 19910827

AB A recombinant human .beta.-interferon (IFN-.beta.) produced in mammalian cells, whose oligosaccharide component comprises biantennary .gtoreq.60%, triantennary .gtoreq.15%, and tetraantennary 0-5% and contains fucose and .gtoreq.80% sialic acid, is useful for treatment of **tumors**, esp. Kaposi's sarcoma. Thus, recombinant IFN-.beta. was produced in transfected CHO BIC 8622 cells in MEM contg. fetal calf serum and secreted into the medium in a yield of 1 .times. 105-1 .times. 106 IU/L. The IFN-.beta. was purified by liq.-liq. extn. in a PEG 2000-salt soln. system, affinity chromatog. on Blue Dextran FF, metal chelate chromatog. on a Zn2+-loaded chelating Sepharose column, and size exclusion chromatog. on Sephacryl. The product showed a purity of >99% and high stability at -20, +15, or +25.degree. when mixed with buffered human serum albumin and stored for 1-4 wk. Enzymic removal of terminal sialic acid residues diminished the stability.

L248 ANSWER 69 OF 70 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 1992:22108426 BIOTECHNO
TITLE: Suppression and transient induction of lymphokines in **cancer** patients after administration of polyethylene glycolated interleukin-2
AUTHOR: Shih Y.; Konrad M.W.; Warren M.K.; Childs A.; Paradise C.; Meyers F.J.; Groves E.S.
CORPORATE SOURCE: Cetus Corporation, Div Hematology and Oncology, University of California,Davis, CA, United States.
SOURCE: European Journal of Immunology, (1992), 22/3 (727-733) CODEN: EJIMAF ISSN: 0014-2980
DOCUMENT TYPE: Journal; Article
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Polyethylene glycolated (**pegylated**) interleukin-2 (**PEG** IL-2) was administered as a weekly i.v. bolus to patients with metastatic **cancer** in a phase-I trial. Efficacy, toxicity and pharmacokinetics have been described previously. To explore mechanism of IL-2 action and discover predictors of efficacy, the levels of several lymphokines were measured in pharmacokinetic scrum samples. IL-1.beta. and IL-6 were elevated in many patients before **PEG** IL-2 administration, forming a continuous, log-normal distribution among patients. The levels of the two lymphokines were strongly correlated. However, no significant correlation could be found between these levels, clinical chemistry, or **tumor** regression seen after **PEG** IL-2 administration. Three hours after **PEG** IL-2 administration, IL-1.beta. and IL-6 levels, if elevated, fell to normal. In all patients, independent of initial levels, IL-6 and IFN-.gamma., but not IL-1.beta., increased 4 to 6 h after the injection and then fell rapidly, even though **PEG** IL-2 levels were high and often changed only slightly during this period. This suggests an active shut down of lymphokine synthesis, or an increase in elimination rate. After the fourth administration of **PEG** IL-2, the peak level of IFN-.gamma. was 2 to 20 times higher

than after the first, while the peak level of IL-6 did not change in a consistent direction. Responding patients had typical peak levels of IL-6 and IFN-.gamma.. Low levels of TNF and IL-4 were occasionally seen before and after **PEG** IL-2 administration. but no consistent pattern was evident.

L248 ANSWER 70 OF 70 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 1990:20291104 BIOTECHNO
TITLE: Anti-**tumor** protection induced in mice by fatty acid conjugates: Alkyl butyrates and **poly(ethylene glycol)** dibutyrates
AUTHOR: Wakselman M.; Cerutti I.; Chany C.
CORPORATE SOURCE: INSERM, Unite 43, Hopital St Vincent de Paul, 74 Avenue Denfert-Rochereau,75674 Paris Cedex 14, France.
SOURCE: International Journal of Cancer, (1990), 46/3 (462-467)
CODEN: IJCNAW ISSN: 0020-7136
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Simple fatty acids, especially butyrate salts, have interesting biological properties, since they are able to down-regulate cell growth and promote various differentiated cellular functions. Their use for anti-**tumor** treatment is, however, hampered by their over-rapid diffusion in the blood, followed by a short-lived biological action. We have therefore devised conjugates linking butyrate with either (i) alipathic alcohols of increasing carbon numbers ranging from C.sub.4 to C.sub.1.sub.2 or (ii) poly(ethylene glycols) of increasing molecular weights. In both cases, the resulting butyric esters can be hydrolysed by esterases which can release biologically active subunits from the synthetic compounds. As shown in the present study, only one conjugate in each series gave satisfactory anti-**tumor** protection: namely, 1-octyl butyrate and **poly(ethylene glycol** 1000) dibutyrate respectively. A single immune-stimulatory injection of purified Corynebacterium parvum extract prior to administration of the conjugates significantly increased the anti-**tumor** potency.

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L240 ANSWER 1 OF 13 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:916534 PROMT
TITLE: Schering-Plough Projects 2001 and 2002 Earnings, Highlights Business Progress, Strong Product Pipeline.
SOURCE: PR Newswire, (21 Dec 2001) pp. NYF07121122001.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 2316
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX In . . . said, "In 2001, we gained marketing approvals both in the United States and the European Union for CLARINEX and for **PEG-INTRON** and REBETOL combination therapy, as well as approval of REBETOL in Japan, the world's second-largest pharmaceutical market. These products, competing. . .

"With the approval of **PEG-INTRON** and REBETOL combination therapy, Schering-Plough continues its leadership in developing and bringing to market significant advances in the treatment of. . . worldwide," Kogan said. In 2001, the company launched in both the United States and the European Union combination therapy using **PEG-INTRON**(TM) (**peginterferon** alfa-2b) Powder for Injection and REBETOL(R) (ribavirin, USP) Capsules for treating chronic hepatitis C. **PEG-INTRON** provides superior efficacy to INTRON(R) A (interferon alfa-2b, recombinant) in treating hepatitis C, and its convenient once-weekly dosing may enhance. . . compliance. . . . for use only in combination with INTRON A for the treatment of chronic hepatitis C. Phase III clinical studies with **PEG-INTRON** are ongoing in Japan.

In the United States, post-marketing studies with **PEG-INTRON** and REBETOL are ongoing to better define optimal treatment regimens using these therapies and further explore their use in treating. . .

Schering-Plough Research Institute is also exploring new market opportunities for existing products. **PEG-INTRON**, approved as monotherapy and in combination with REBETOL for treating hepatitis C, is in Phase III development for two cancer. . .

In . . . for treating patients with acute coronary syndrome, including patients who are being managed medically and those undergoing percutaneous coronary intervention. **TEMODAR**(R) (temozolomide), approved for treating certain types of brain cancer, is in Phase II studies for treating a variety of solid. . .

L240 ANSWER 2 OF 13 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:779169 PROMT
TITLE: Sales flat at Schering-Plough as manufacturing problems persist.
SOURCE: Marketletter, (29 Oct 2001) .
ISSN: 0951-3175.
PUBLISHER: Marketletter Publications Ltd.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 208
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX **Temodar** (temozolomide), S-P's treatment for certain types of brain tumors, saw turnover rise 20% to $45 million, while sales of the. . .

However, combined sales of the antiviral/anticancer drugs Intron A (**interferon** alfa-2b), **Peg-Intron** (**peginterferon** alfa-2b), Rebetol (ribavirin) and Rebetron (Intron A + Rebetol) declined 11% to $301 million, primarily as a result of manufacturing. . .

L240 ANSWER 3 OF 13 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:767772 PROMT
TITLE: Schering-Plough Reports Sales, Earnings for 2001 Third Quarter, First Nine Months.
SOURCE: PR Newswire, (23 Oct 2001) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 2041
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX In . . . the INTRON(R) A franchise totaled $301 million, down 11 percent versus the comparable year-ago period. The franchise includes INTRON A (**interferon** alfa-2b); **PEG-INTRON** (TM) (**peginterferon** alfa-2b), a longer-acting form of INTRON A (as monotherapy and, internationally, in combination with REBETOL(R) (ribavirin, USP) Capsules for treating. . .

Third quarter worldwide sales of **TEMODAR**(R) (temozolomide), for treating certain types of brain tumors, were $45 million, up 20 percent. Sales of INTEGRILIN(R) (eptifibatide) Injection, a. . .

U.S. . . . In anti-infective/anticancer, U.S. sales of the INTRON A franchise totaled $129 million, down 30 percent. Third quarter domestic sales of **TEMODAR** rose to $23 million, up 12 percent. In cardiovasculars, domestic sales of INTEGRILIN increased 10 percent to $53 million. In. . .

International . . . franchise totaled $172 million, up 13 percent versus the comparable 2000 period. Also contributing to third quarter international sales were **TEMODAR**, with sales of $21 million, up 32 percent, and REMICADE, with sales of $42 million. Worldwide sales of animal health. . .

Sales . . . The overall sales decline for U.S. pharmaceuticals was moderated by higher sales of CLARITIN, NASONEX, PROVENTIL and other albuterol products, **TEMODAR** and INTEGRILIN.

International . . . CLARITIN and CLARINEX, and NASONEX in allergy/respiratory. Also contributing to higher international sales in the 2001 first nine months was **TEMODAR**.

Temodar 45 37 20 132 89 49

*The INTRON A franchise includes INTRON A, **PEG-INTRON** (monotherapy for treating hepatitis C and, internationally, in combination with REBETOL), and REBETRON Combination Therapy.

L240 ANSWER 4 OF 13 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:560634 PROMT
TITLE: Flat 2nd-qtr sales/EPS at Schering-Plough.(Brief Article)
SOURCE: Marketletter, (30 Jul 2001) .
ISSN: 0951-3175.
PUBLISHER: Marketletter Publications Ltd.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 244
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX Second-quarter . . . for Claritin (loratadine), which grew 3% to $925

million, and Nasonex (mometasone furoate) nasal spray, up 51% to $183 million. **Temodar** (temozolomide) turnover rose 46% to $44 million, while that of Integrilin (eptifibatide) Injection increased 60% to $67 million and Remicade. . .

However, combined sales of the antiviral/anticancer drugs Intron A (**interferon** alfa-2b), **Peg-Intron** (**peginterferon** alfa-2b), Rebetol (ribavirin) and Rebetron (Intron A + Rebetol) declined 13% to $315 million.

L240 ANSWER 5 OF 13 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:555573 PROMT
TITLE: Schering-Plough Reports Sales, Earnings for 2001 Second Quarter, First Half.
SOURCE: PR Newswire, (25 Jul 2001) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 2135
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX In . . . anti-infective/anticancer INTRON(R) A franchise totaled $315 million, down 13 percent versus the comparable year-ago period. The franchise includes INTRON A (**interferon** alfa-2b); **PEG-INTRON**(TM) (**peginterferon** alfa-2b), a longer-acting form of INTRON A (as monotherapy for treating hepatitis C and, internationally, in combination with REBETOL(R) (ribavirin,. . .

Second quarter worldwide sales of **TEMODAR**(R) (temozolomide), for treating certain types of brain tumors, were $44 million, up 46 percent. Sales of INTEGRILIN(R) (eptifibatide) Injection, a. . . In anti-infective/anticancer, U.S. sales of the INTRON A franchise totaled $147 million, down 32 percent. Second quarter domestic sales of **TEMODAR** rose to $26 million, up 55 percent. Sales of cardiovascular products in the 2001 second quarter were down 24 percent. . .

International . . . totaled $169 million, up 16 percent versus the comparable 2000 period, benefiting from the March 2001 European Union approval of **PEG-INTRON** and REBETOL combination therapy for the treatment of chronic hepatitis C. Also contributing to second quarter international sales were **TEMODAR**, with sales of $18 million, up 34 percent, and REMICADE.

Sales . . . due to continued generic competition. The overall sales decline for U.S. pharmaceuticals was moderated by higher sales of CLARITIN, NASONEX, **TEMODAR** and INTEGRILIN.

International . . . foreign exchange is excluded) and totaled $1.6 billion. Higher sales were led by NASONEX, the INTRON A franchise, REMICADE and **TEMODAR**.

Temodar 44 30 46 87 51 69

* The Intron A franchise includes INTRON A, **PEG-INTRON** (monotherapy for

L240 ANSWER 6 OF 13 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:494281 PROMT
TITLE: Schering-Plough Reviews Pharmaceutical Research and Business Progress.
SOURCE: PR Newswire, (28 Jun 2001) pp. 4844.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English

WORD COUNT: 2451
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX In . . . the anticancer/antiviral agent INTRON(R) A (interferon alfa-2b, recombinant); REBETRON(TM) Combination Therapy, containing REBETOL(R) (ribavirin) Capsules and INTRON A Injection; and **PEG-INTRON**(TM) (**peginterferon** alfa-2b), a longer- acting form of INTRON A and the world's first **pegylated interferon** on the market. "No other company has done more to develop and introduce new treatments for hepatitis C than Schering-Plough,". . .

Reviewing . . . market in Europe; TEQUIN(TM) (gatifloxacin), a new broad-spectrum antibiotic for respiratory infections co-promoted in the United States with Bristol-Myers Squibb; **TEMODAR**(R) (temozolomide), an oral agent approved in the EU and United States for treating certain types of brain cancer; and CAELYX(R),. . .

Dr. . . . Combination Therapy, which produces a three-fold increase in sustained response rates compared with INTRON A monotherapy, and the development of **PEG-INTRON**, which offers patients the convenience of once-weekly injections. He said **PEG-INTRON**/REBETOL combination therapy can raise the sustained viral response rate for all hepatitis C genotypes to 54 percent and, in particular, can significantly improve response rates in the poor prognosis genotype 1 patients. He noted that the **PEG-INTRON** /REBETOL combination therapy, approved in the EU and under priority review in the United States, represents the new standard of care. . .

In . . . said Doliveux. In reviewing product sales in Europe, Doliveux said growth was being driven by INTRON A and REBETOL, REMICADE, **TEMODAR**, NASONEX and CLARINEX. Doliveux said CLARINEX has already become the leading nonsedating antihistamine in Germany. NASONEX is the leading nasal-inhaled steroid in Italy, France and Germany, and the fastest-growing product in its therapy class. In anti-infectives/anticancer, he said **PEG-INTRON**/REBETOL combination therapy was launched in major European markets in the second quarter for the treatment of hepatitis C. He also. . .

L240 ANSWER 7 OF 13 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:308802 PROMT
TITLE: Manufacturing woes hit Schering-Plough.
SOURCE: Marketletter, (23 Apr 2001) .
ISSN: 0951-3175.
PUBLISHER: Marketletter Publications Ltd.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 290
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX Pharmaceutical . . . its major therapeutic categories except anti-infectives/cancer, where increases were registered. Nevertheless, in the latter sector, combined sales of Intron A (**interferon** alfa-2b), **Peg-Intron** (**peginterferon** alfa-2b), a longer-acting form of Intron A, and Rebetron combination therapy containing Intron A and Rebetol (ribavirin) totaled $326 million,. . .

Also making a positive contribution to the quarter's sales were: **Temodar** (temozolomide) for the treatment of certain brain tumors, adding $43 million; Integrilin (eptifibatide), a therapy for patients with acute coronary. . .

L240 ANSWER 8 OF 13 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:297991 PROMT
TITLE: Schering-Plough Reports Sales, Earnings for 2001 First Quarter.
SOURCE: PR Newswire, (17 Apr 2001) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 1577
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX In . . . a once-daily nasal-inhaled steroid for allergies, increased 13 percent to $92 million. Combined sales of the anti-infective/anticancer agent INTRON(R) A (**interferon** alfa-2b); **PEG-INTRON**(TM) (**peginterferon** alfa-2b), a longer-acting form of INTRON A; and REBETRON(TM) Combination Therapy containing INTRON A and REBETOL(R) (ribavirin, USP) Capsules, totaled. . .

Also contributing to first quarter worldwide sales were **TEMODAR** (R) (temozolomide), for treating certain types of brain tumors, with sales of $43 million; INTEGRILIN(R) (eptifibatide) Injection, a glycoprotein platelet aggregation. . .

U.S. . . . predecessor nasal-inhaled steroid for allergies, were down sharply due to manufacturing issues. In anti-infective/anticancer, U.S. combined sales of INTRON A, **PEG-INTRON** and REBETRON Combination Therapy totaled $187 million, down 4 percent, reflecting a slowing in the hepatitis C market attributable to. . . antifungal/anti-inflammatory, were down due to changes in the timing of trade buying. Reflecting increased utilization, first quarter domestic sales of **TEMODAR** rose to $26 million and, in cardiovasculars, sales of INTEGRILIN increased 30 percent to $34 million.

International . . . million. International sales were led by, in allergy/respiratory, NASONEX, with sales of $29 million, up 52 percent; and, in anti-infective/anticancer, **TEMODAR**, with sales of $17 million, up 58 percent, and REMICADE. International combined sales of INTRON A (including combination therapy with REBETOL and **PEG-INTRON**) totaled $139 million, down 2 percent versus the comparable 2000 period.

Temodar 43 21
N/M

L240 ANSWER 9 OF 13 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2001:66246 PROMT
TITLE: Schering-Plough Reports Sales, Earnings for 2000 Fourth Quarter and Full Year.
SOURCE: PR Newswire, (25 Jan 2001) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 1905
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX Worldwide . . . 1 antihistamine, grew 15 percent to $662 million. Combined 2000 fourth quarter sales of the anti- infective/anticancer agent INTRON(R) A (**interferon** alfa-2b); **PEG-INTRON** (TM) (**peginterferon** alfa-2b), a longer-acting form of INTRON A; and REBETRON(TM) Combination Therapy containing INTRON A and REBETOL(R) (ribavirin, USP) Capsules, totaled. . . Injection, a glycoprotein platelet aggregation inhibitor for the treatment of patients with acute coronary syndromes, with sales of $50 million; **TEMODAR**(R) (temozolomide), for treating certain types of brain tumors, with sales of $33 million, up 73 percent; and REMICADE(R) (infliximab), for. . .

U.S. . . . were sharply higher at $46 million, driven by increased market penetration. Also contributing to higher fourth quarter domestic sales was **TEMODAR**, with sales of $17 million.

International . . . in allergy/respiratory, the CLARITIN line and NASONEX, and, in anti- infective/anticancer, by INTRON A (including combination therapy with REBETOL) and **PEG-INTRON**.
Also contributing to higher international sales were **TEMODAR** and REMICADE.

The . . . line, up 13 percent to $3.0 billion. Combined 2000 worldwide sales of INTRON A (including combination therapy with REBETOL) and **PEG-INTRON**, totaled $1.4 billion, up 21 percent.
Worldwide 2000 sales of the company's nasal inhaled steroid franchise increased 24 percent to. . . sales up 60 percent to $415 million. Also contributing to higher 2000 sales were INTEGRILIN, with sales of $172 million; **TEMODAR**, with sales of $121 million; and REMICADE, with sales of $57 million.

U.S. . . . release of positive results from a major clinical trial in early 2000. Also contributing to higher 2000 domestic sales was **TEMODAR**, with sales of $65 million.

International . . . is excluded). Higher international sales were led by the CLARITIN line, NASONEX, INTRON A (including combination therapy with REBETOL) and **PEG-INTRON**. Also contributing to higher international sales were **TEMODAR** and REMICADE. Worldwide sales of animal health products in 2000 totaled $720 million, up 7 percent (12 percent when foreign. . .

Temodar	33	19	73	121	36

N/M

* Includes international sales of **PEG-INTRON**.

L240 ANSWER 10 OF 13 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2000:978409 PROMT
TITLE: Schering-Plough Annual Meeting Highlights Worldwide Performance, Commitment to Pharmaceutical Research.
SOURCE: PR Newswire, (25 Apr 2000) pp. 5365.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 978
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX U.S. and European Union (EU) marketing clearances were received for **TEMODAR**(R) (temozolomide), an oral treatment for certain types of brain tumors, expanding the company's portfolio of anticancer treatments.
-In the anti-infective/anticancer category, **PEG-INTRON** (R), a longer-acting form of INTRON A, is under U.S. and EU regulatory review as a monotherapy for the treatment of hepatitis C, and is being developed as a combination therapy with REBETOL for hepatitis C. **PEG-INTRON** is also being developed as a potential cancer therapy to treat a variety of solid tumors. Another anticancer product in. . .

L240 ANSWER 11 OF 13 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2000:917937 PROMT
TITLE: Schering-Plough Reports Sales, Earnings for 2000 Third Quarter, First Nine Months.
SOURCE: PR Newswire, (24 Oct 2000) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English

WORD COUNT: 1462
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX In . . . No. 1 antihistamine, rose 10 percent to $787 million. Combined third quarter worldwide sales of the antiviral/anticancer agent INTRON(R) A (**interferon** alfa-2b); **PEG-INTRON** (TM) (**peginterferon** alfa-2b), a longer-acting form of INTRON A; and REBETRON(TM) Combination Therapy containing INTRON A and REBETOL(R) (ribavirin, USP) Capsules, totaled. . . INTEGRILIN(R) (eptifibatide) Injection, a platelet aggregation inhibitor for the treatment of acute coronary syndromes, with sales of $52 million, and **TEMODAR**(R) (temozolomide), for treating certain types of brain tumors, with sales of $37 million.

U.S. . . . to $78 million. Other products contributing to higher third quarter domestic sales were INTEGRILIN, with sales of $48 million, and **TEMODAR**, with sales of $21 million.

International . . . (19 percent when foreign exchange is excluded). Sales growth was led by INTRON A (including combination therapy with REBETOL) and **PEG-INTRON**, which combined rose 41 percent to $153 million, and NASONEX, with sales of $20 million. Also contributing to higher international sales were **TEMODAR** and REMICADE(R)(infliximab), for the treatment of rheumatoid arthritis and Crohn's disease.

Sales . . . CLARITIN, NASONEX and INTRON A/REBETRON Combination Therapy. Also contributing to higher sales in the first nine months were INTEGRILIN and **TEMODAR**.

International . . . (15 percent when foreign exchange is excluded). Higher sales were led by INTRON A (including combination therapy with REBETOL) and **PEG-INTRON** in anti-infective/anticancer and by NASONEX in allergy/respiratory. Also contributing to higher international sales in the first nine months were **TEMODAR** and REMICADE.

L240 ANSWER 12 OF 13 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2000:636596 PROMT
TITLE: Schering-Plough Reports Sales, Earnings for 2000 Second Quarter, First Half.
SOURCE: PR Newswire, (25 Jul 2000) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 1376
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX Worldwide . . . mcg, a once-daily nasal steroid for allergies. Also contributing to higher second quarter worldwide sales by category were: in anti-infective/anticancer, **TEMODAR**(R) (temozolomide), an oral treatment for certain types of brain tumors, and, in cardiovasculars, INTEGRILIN(R) (eptifibatide) Injection, a platelet aggregation inhibitor. . .

In . . . 2000 second quarter. Other products contributing to higher second quarter domestic sales by category were: in allergy/respiratory, NASONEX; in anti-infective/anticancer, **TEMODAR**; and, in cardiovasculars, INTEGRILIN.

International . . . to $788 million. Products contributing to higher second quarter international sales were NASONEX, INTRON A (including combination therapy with REBETOL), **TEMODAR** and REMICADE(R) (infliximab), marketed for Crohn's disease. The company also continued to expand its sales force in major international markets to support current product lines and the recent launches of REMICADE for the treatment of rheumatoid arthritis and **PEGINTRON**(TM) (**peginterferon**

alfa-2b), a longer-acting form of INTRON A, for the treatment of chronic hepatitis C.

Sales . . . 1999 first half. Sales growth was led by CLARITIN and NASONEX in the allergy/respiratory category; INTRON A/REBETRON Combination Therapy and **TEMODAR** in the anti-infective/anticancer category; and INTEGRILIN in cardiovasculars.

International . . . sales were led by CLARITIN and NASONEX in the allergy/respiratory category and INTRON A (including combination therapy with REBETOL) and **TEMODAR** in the anti-infective/anticancer product category.

L240 ANSWER 13 OF 13 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2000:169630 PROMT
TITLE: Plowing along.
AUTHOR(S): Brown, Joseph
SOURCE: Med Ad News, (Sept 1999) Vol. 18, No. 9, pp. 248. ISSN: 1067-733X.
PUBLISHER: Engel Publishing Partners
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 5039
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX In . . . treatment of adults with refractory anaplastic astrocytoma. The product will be marketed in the United States under the brand name **Temodar**. **Temodar** is the first new chemotherapy agent for this type of brain tumor to be approved in the United States in. . .

Analysts predict that **Temodar**/Temodal will generate $30 million in sales in 1999, $85 million in 2000, $115 million in 2001, and $150 million in. . .

Schering-Plough . . . to build up its anti-infective and anticancer portfolio. The company is developing a longer-acting, pegylated version of Intron A, called **PEG-Intron** A (**interferon** alfa-2b). The product's clinical development includes Phase III clinical trials for treating malignant melanoma and chronic myelogenous leukemia, and Phase I clinical trials for treating a variety of solid tumors. In addition, **PEG-Intron** A is in Phase III clinical trials for treating hepatitis C as monotherapy and in combination with Rebetol. **PEG-Intron** A uses the Pegnology protein-based drug delivery system developed by Euzon Inc., Piscataway, N.J.

Analysts . . . HKS say Schering-Plough will be able to expand the market for Intron A if the company is able to prove **PEG-Intron** A is superior to Intron A. Without any major benefits over Intron A, the analysts believe that **PEG-Intron** A will cannibalize Intron A's market share.

* Schering-Plough revised its license agreement with Enzon Inc. (Nasdaq: ENZN) for **PEG-Intron** A, which entitled Enzon to royalties for product sales and specific milestone payments. The revised agreement calls for Schering-Plough to. . .

* **Temodar**/Temodal, for glioblastoma multiforme